Risks of future harm in adolescents hospitalised with violent, self-inflicted or drug/alcohol-related injury

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Declaration

I, Annie Herbert, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Abstract

Background: Information is lacking on the risks of future harm for adolescents hospitalised in England as an emergency with adversity-related injury (violent, self-inflicted, drug/alcohol-related). Evidence is needed on who is most at risk and the types of harm, to inform preventive strategies.

Methods: Using Hospital Episode Statistics linked to Office for National Statistics mortality data for England (April 1997-March 2012), I estimated the prevalence of emergency admissions for adversity-related injury among 10-19y olds, and identified risk factors. I examined the risks of death and emergency re-admission after discharge from adversity-related injury, compared with after accident-related injury.

Results: 1 in 25 adolescents had an emergency admission for adversity-related injury between the ages of 10 and 19y. Among these adolescents, 73% of girls and 38% of boys were admitted with more than one type (e.g., self-inflicted and drug/alcohol-related). In addition, 1/137 girls and 1/64 boys with adversity-related injury died within ten years after discharge; 54% of girls and 41% of boys were re-admitted as an emergency. These risks were approximately double those following accident-related injury, regardless of whether violent, self-inflicted or drug/alcohol-related, and were particularly high for older boys and adolescents with chronic conditions. Increased risks of death were mostly explained by suicide and drug/alcohol-related deaths. After each type of adversity-related injury, risks of drug/alcohol-related deaths were similar to those of suicide deaths.

Conclusions: 1 in 25 adolescents in England were admitted as an emergency to hospital for adversity-related injury, often with multiple types of adversity-related injury, and were at considerable risks of harm in the next decade compared to other adolescents. Current strategies to reduce risks after self-inflicted injury in this group should be extended to violent and drug/alcohol-related injury. Strategies could include targeting older adolescents with chronic conditions, and prioritising risks of drug/alcohol-related death alongside those of suicide death.

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Abbreviations

CAMHS – Community Adolescent Mental Health Services

CI – Confidence Interval

CIF – Cumulative Incidence Function

DH – Department of Health

ED – Emergency Department ('Accident & Emergency')

GP – General Practitioner

HES – Hospital Episode Statistic

HR – Hazard Ratio

KM – Kaplan-Meier

NICE – National Institute for Clinical Excellence

ONS – Office for National Statistics

OR – Odds Ratio

PCT – Primary Care Trust

PH – Proportional Hazards

PL – Partial Likelihood

PWP – Prentice, Williams & Peterson

RCT – Randomised Controlled Trial

UK – United Kingdom

US – United States

WHO – World Health Organization

WLW – Wei, Lin & Weissfeld

YP – Young Person

Notation

$\boldsymbol{\beta}$ = $(\beta_1, \beta_2, \ldots \beta_p)$ = beta coefficients of covariates $\boldsymbol{X}$

$\gamma(\,)$ = hazard for non-terminal endpoint

$\lambda(\,)$ = hazard for terminal endpoint

π = acceleration parameter in accelerated failure time models

ω_i = frailty for subject i

$CIF_c(\,)$ = cumulative incidence function from cause c

c = cause ID $(c = 1, \ldots v)$

d_j = number of events at t_j

D_j = set of subjects that have an event at t_j

$\boldsymbol{\varepsilon}$ = $(e_1, e_2, \ldots e_w)$ = model residuals

$f(\,)$ = failure function; $F(\,)$ = cumulative failure function

$h(\,)$ = hazard function; $h_0(\,)$ = baseline hazard; $\bar{h}_c(\,)$ = sub-hazard of event through cause c; $\bar{h}_c(\,)$ = cause-specific hazard of event through cause c; $H(\,)$ = cumulative hazard function

i = subject ID $(i = 1, \ldots n)$

j = time-point ID $(j = 1, \ldots \tau)$

k = event order for subject i $(k = 1, \ldots m_i)$

l = event ID $(l = 1, \ldots L)$

R_j = set of subjects at risk of an event at t_j ('risk-set')

s_j = sum of covariate values across all subjects who have an event at t_j

$S(\,)$ = survival function

T = failure time variable ($T*$ observed failure times)

t = time variable; t_0 denotes time at entry (usually 0)

$PPL(\,)$ = partial likelihood

u = covariate ID $(u = 1, \ldots p)$

$\boldsymbol{X}$ = $(x_1, x_2, \ldots x_p)$ = covariates, e.g. sex or age

Statement about funders

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Chapter 1 Thesis background and rationale

1.1 Chapter summary

Chapter 1 describes the rationale for studying adolescents who present to hospital with adversity-related injury. Throughout this thesis, ‘adolescent’ refers to children and young people aged 10-19 years old, and ‘adversity-related injury’ any violent, self-inflicted, or drug/alcohol-related injury.

In Section 1.3, I discuss why adolescents are a vulnerable population, the common occurrence (and definition) of violent, self-inflicted, and drug/alcohol-related injuries, and why emergency presentations to hospital for these injuries are the focus of interest for this thesis. In Section 1.4, I summarise the evidence on the frequency of presentations for adversity-related injury among adolescents in England. In Section 1.5, I report findings from a systematic review of the literature on the risks of future harm following such presentations. Finally in Section 1.6, I provide an overview of several systematic reviews of randomised controlled trials, of hospital-based interventions to reduce these risks.

There is a lack of evidence about adolescents who are hospitalised with more than one type of adversity-related injury (violent, self-inflicted, drug/alcohol-related). These three types are often related to similar underlying psychosocial problems, such as adverse childhood experiences, and there is some evidence of an ‘overlap’ across these types at least for adolescents in the general population (e.g. many adolescents exposed to self-inflicted injury will have also misused drugs/alcohol). It is essential to gather evidence on the occurrence of all three types of adversity-related injury from the same sample of adolescents, as it is otherwise difficult to understand their inter-relationship.

It is also important to understand the extent to which the same adolescents are admitted with multiple types of adversity-related injury, or whether risks of future harm differ according to the three types. Current national guidelines for management of presentations for self-inflicted injury mandate admission for young adolescents and psychosocial assessment for all patients, recommendations which do not extend to corresponding guidelines for violent or drug/alcohol-related injury. Information about adolescents hospitalised for all three types of adversity-related injury could also inform development of interventions for these presentations. This conclusion leads to the aims and objectives of this thesis, which are discussed in Chapter 2.

1.2 Introduction

This chapter provides a rationale for studying adolescents who present to hospital with 'adversity-related injury' (violent, self-inflicted, or drug/alcohol-related injury). It also reviews the existing evidence on the prevalence of and risk factors for different types of adversity-related injury among adolescents who present to hospitals in England as an emergency, as well as associated risks of harm following such presentations. Finally, the chapter provides an overview of the effectiveness of interventions that may be employed for reducing risks of future harm.

1.3 Importance of adversity-related injury among adolescents

1.3.1 Why adolescents?

The World Health Organization (WHO) defines 'adolescents' as 10-19 year olds (representing 12% of the UK population in 2013) and 'young people' as 10-24 year olds (19%) (1). Despite the common belief that adolescents and young people are in a healthy period of life (2), they are a vulnerable group for psychological problems, and uptake of risky behaviours. Yet they are also increasingly recognised as a relatively neglected age-group in public health policies (3-5).

Figure 1.1 illustrates how vulnerability during adolescence may be associated with poor physical health or psychosocial outcomes later in adolescence and adulthood. Adolescents experience stresses unique to their age-group, including puberty, increasing independence from parental supervision, and increasing exposure to social interactions. Adolescence is a time when a large proportion of individuals first adopt or are exposed to risky or poor health behaviours such as violence, self-harm, binge drinking, drug-taking, smoking, risky sexual behaviours, or crime (6-9). For example, in the Health Behaviours in School Children (HBSC) survey in England (9), 12% of children had already had an alcoholic drink by 11 years old, increasing to 74% by 15 years old. Adolescents who are not yet fully mentally or socially developed, and those with mental health problems, are particularly vulnerable to these stresses (10, 11). In addition, half of all cases of mental disorders such as anxiety start before 14 years old, and three-quarters before age 24 (12).

Evidence from cohort studies of adolescents and young people in the general population suggests that those who have mental health issues or adopt risk-taking behaviours are at increased risks of harm, both during adolescence and later in the life-course, compared to those who do not (13-16). For the example in Figure 1.1 of adolescents who are exposed to alcohol misuse, there is evidence to show that these adolescents are at increased risks of illicit drug use and dependence, heavy smoking and drinking, and chronic mental health problems before the age of 25 (14). These adolescents are also at increased risks of hospital admissions for accidents or chronic physical or mental illness and of mortality in young to mid-adulthood (different studies have reported increased risks over a range of 25-47 years old) (14).

There is evidence to suggest that programmes that target adolescents and young people with mental health issues and risk-taking behaviours, can be effective for reducing the incidence of these issues and behaviours, and thus associated morbidity and mortality(17). Such issues and behaviours are likely to be less entrenched during adolescence compared with young people (20-24 year olds). For example, the younger an individual initiates alcohol use, the more likely he or she is to develop a chronic alcohol disorder or engage in other risk-taking behaviours, such as violence (14, 18).

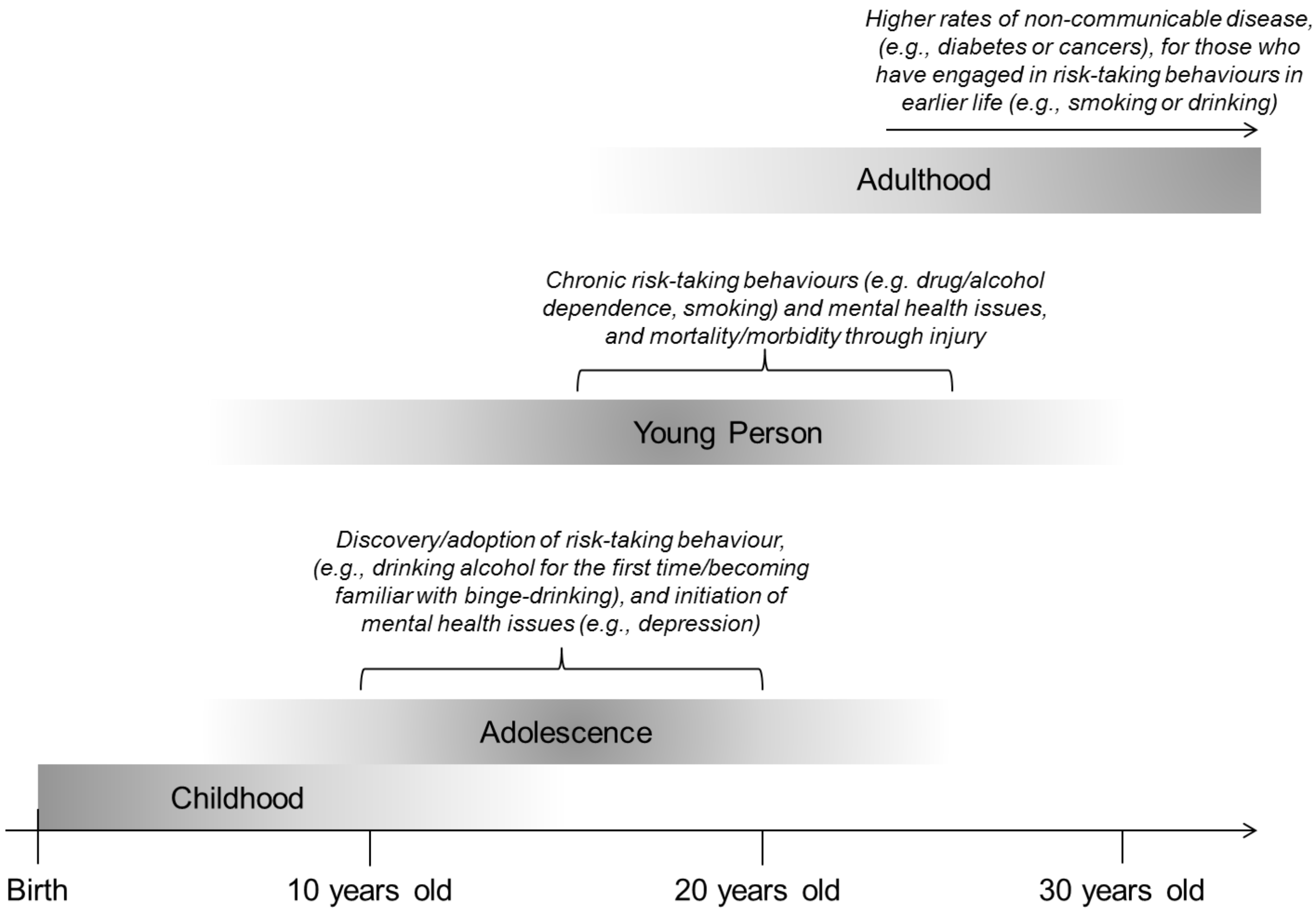
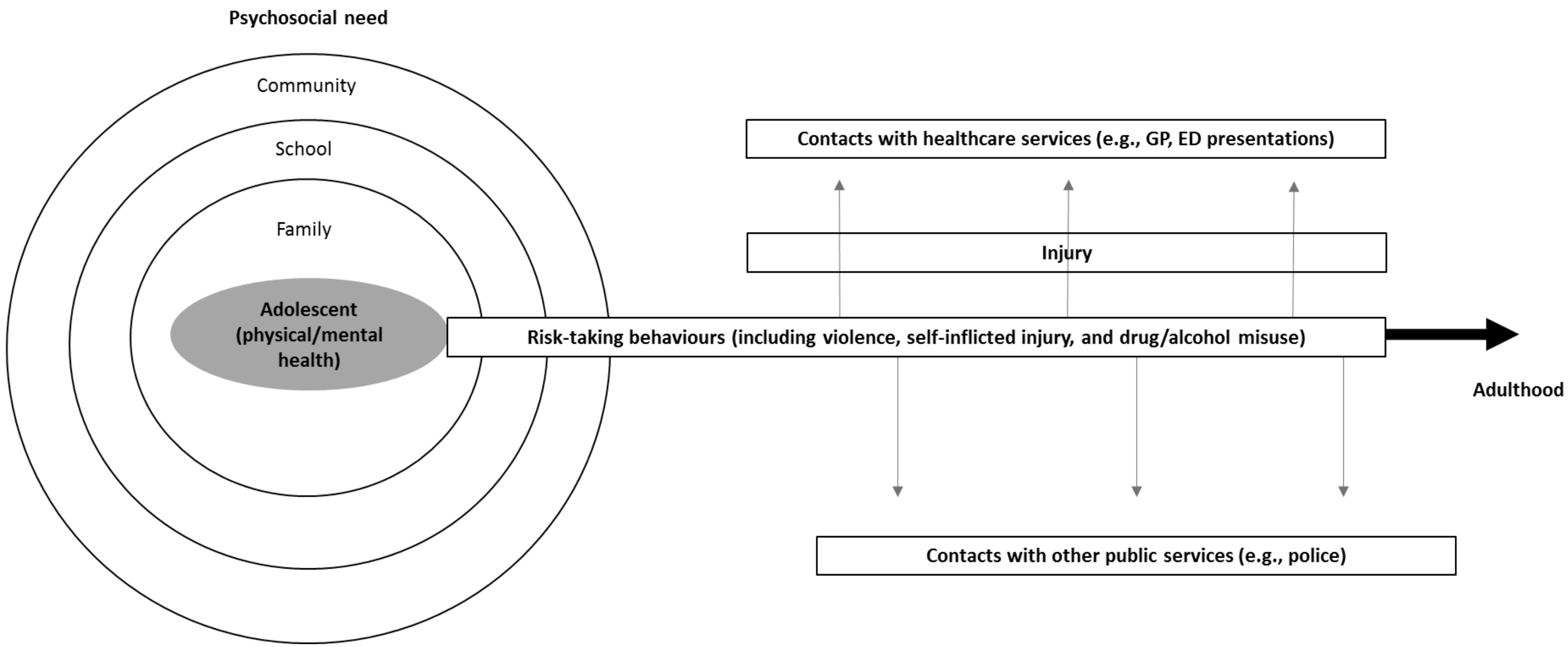


Figure 1.1: Conceptual diagram of adoption of risk-taking behaviours during adolescence and related morbidity or mortality with increasing age

1.3.2 Why violent, self-inflicted and drug/alcohol-related injury?

Figure 1.2 presents how an adolescent's adverse psychosocial circumstances may result in contacts with healthcare or other public services. 'Adversity' may refer to any harm or the potential for harm to an adolescent's health. Such adversity can encompass home, school, or neighbourhood environmental factors, chronic disease, or engagement in or exposure to risk-taking behaviours (13, 19, 20).

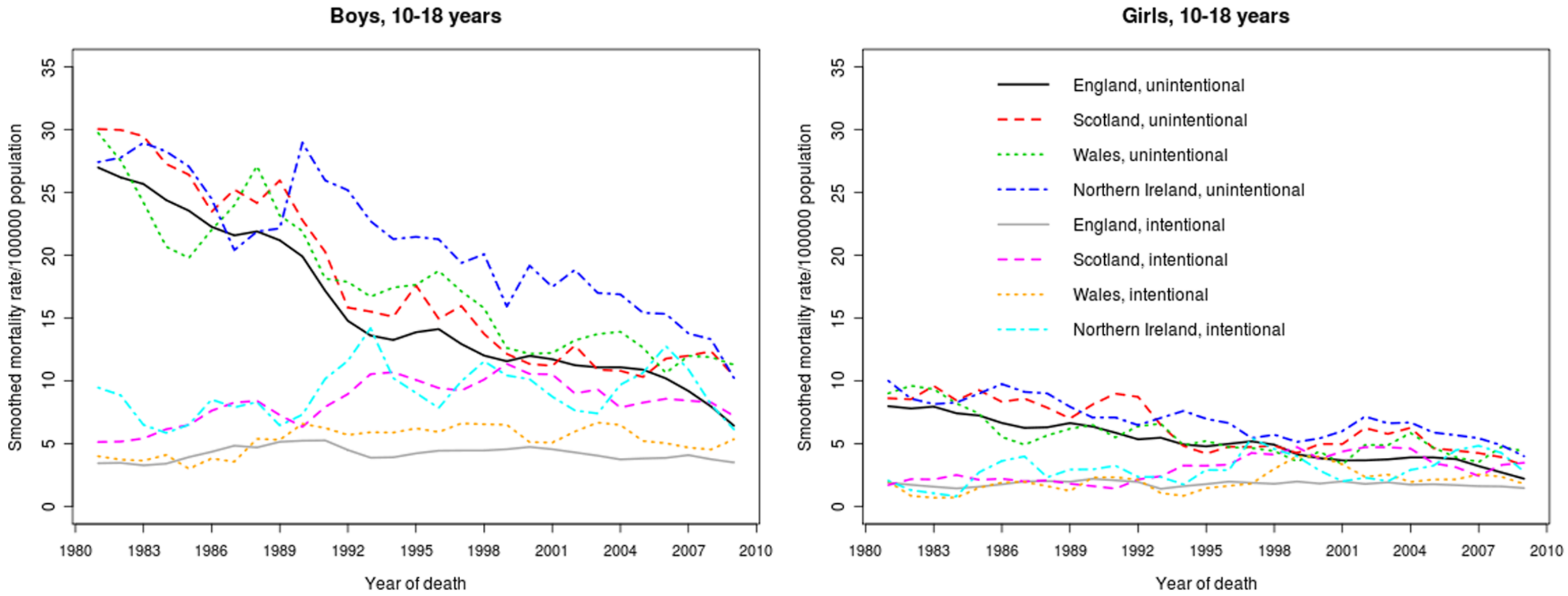
In this thesis, I use the term 'adversity' to mean violence, self-harm or drug/alcohol misuse. I focus on these three exposures because they are common risk-taking behaviours among adolescents (6, 9, 20, 21), and account for a large proportion of hospitalisations and mortality for injury in this age-group (22-24). Presentations to hospital can represent a 'teachable moment' with which to intervene and reduce suffering and risks of future harm (25, 26).



ED = Emergency Department; GP = General Practitioner

Figure 1.2: Conceptual diagram of the relationship between adolescent psychosocial need and health/public service contacts

As Figure 1.3 shows, rates of mortality through intentional injuries (i.e., those related to violence, self-inflicted injury and events of undetermined intent) for adolescents in England, have changed little in the past 30 years (27). This is in contrast to substantial declines in rates of mortality through unintentional injury, (i.e., traffic accidents, other injuries and complications through medical care). For example, for 10-18 year old boys (Figure 1.3, left-hand plot), rates of mortality through intentional injuries have remained at ~4 per 100,000 between 1980 and 2010, but those through unintentional injury have decreased from ~27 to ~6 per 100,000. That is, intentional, potentially preventable, injury now accounts for almost as many deaths as unintentional injury.



Reproduced from Hardelid *et al*, Plos One 2013 (17). Image reproduced with permission of the rights holder, *Plos*.

Figure 1.3: Rates of mortality through unintentional and intentional injuries, among 10-18 year olds in the four UK countries, 1980-2010

1.3.3 Defining violent, self-inflicted and drug/alcohol-related injury

The United Nations Convention on the Rights of the Child (or 'UNCRC') considers **violence** to include "all forms of physical or mental violence, injury or abuse, neglect or negligent treatment, maltreatment or exploitation, including sexual abuse", whether inflicted by a caregiver or peer (28). The prevalence of past-year violence has been estimated from surveys of 11-17 year olds to range between 6.0% and 31.8% (see Table 1.1; varying by age and sub-type of violence, e.g., physical abuse) (6, 29, 30). Violence is often referred to in the literature as 'victimisation' (31).

Self-inflicted injury or 'deliberate self-harm' involves someone harming themselves in a deliberate and usually hidden way (8), for example, through cutting, or self-poisoning (e.g., taking an overdose of paracetamol). As described in more detail in Table 1.1, a national inquiry of self-inflicted injury among 11-25 year olds in England synthesised evidence across 350 different organisations and concluded that the (lifetime) prevalence for these individuals was approximately 7-8% (8).

Drug and alcohol misuse has been defined by the WHO as any use of drugs or alcohol "for a purpose not consistent with legal or medical guidelines" (32). Alcohol misuse includes any drinking that is harmful to health, including getting drunk. As Table 1.1 describes in more detail, from school surveys of 11-15 year olds in England, the proportion who report to have misused drugs ranges from 1% of 11-15 year olds having ever inhaled 'poppers' (alkyl nitrates) to 24% of 15 year old girls having ever tried cannabis; the proportion who report to have misused alcohol ranges from that 1% of 11 year old girls to 43% of 15 year old girls having ever been drunk twice (varying by sex, age, and whether ever, past year, past 30 days or past four weeks; additionally for drugs, varying by type of drug) (29).

Table 1.1: Comments on definition and prevalence of violence, self-harm and drug/alcohol misuse, among adolescents in the general population in England or UK

Type of adversity	Comments on definition and prevalence
Violence	**Definition:** In young adolescents (e.g., 10-14 year olds), violence is likely to result from maltreatment by caregivers, siblings or peers (31). That is, physical aggression, sexual force, or neglect to meet a child's emotional, physical or educational developmental needs where these resources exist (33). Physical or sexual abuse can directly result in injury, whereas neglect can result in injury due to lack of supervision. In older adolescents, violence is likely to result from physical assault by (or to) peers or strangers, e.g., hitting, pushing, pulling, kicking, strangling, smothering, biting, burning (6, 33). **Prevalence:** From the HBSC survey of 11-15 year olds in England in 2009-2010, it was estimated that among 11 year olds, 6% of girls and 20% of boys were involved in fighting at least three times in the past year (29). These rates were 6% and 9% among 15 year olds. Another survey, of 11-17 year olds in the UK in 2009, estimated rates of past-year physical abuse of 11.5%, past-year sexual abuse of 13.2% and past-year neglect of 16.0% (30). Finally, in a school survey of 11-16 year olds in England in 1999/2000 (6), 20.4% to 31.8% reported habitual fighting, at least monthly.
Self-inflicted injury	**Definition:** Includes purposeful external physical harm, e.g., cutting one's own skin (8), and internal physical harm through ingestion (self-poisoning), e.g., overdose of medication. Cutting was reported to be the most common type of self-harm in 15-16 year olds in schools in England in 2000-2001 (34). However, it is has also been suggested that cutting is less-researched compared to other methods of self-harm (8). **Prevalence**: A national inquiry of self-harm in England gathered evidence about the prevalence of self-harm in young people, and other related factors, from over 350 organisations (8). The inquiry found only three studies which reported prevalence estimates (all surveys in adolescents, one in England (34), the others from Australia and Ireland), and even then only for cutting. The inquiry concluded from these three studies, and taking all of their other conversations with organisations into account that one in 12 (7%) to one in 15 (8%) of 11-25 year olds in the UK have ever self-harmed (8).

(Table 1.1 continued)

Drug/alcohol misuse	**Definition:** Drug misuse may include taking of environmental substances for a purpose other than intended, which could be harmful to health, e.g, ingesting of household bleach or sniffing glue, or taking of illicit (illegal) drugs, e.g., cannabis or heroin. Alcohol misuse includes drinking alcohol in a way that could lead to harm (hazardous drinking), e.g., binge drinking, or to poor development or health problems, e.g., dependency. **Prevalence:** A recurring issue for estimating the prevalence of drug/alcohol misuse is that there is no universal measurement of this. For example, drug misuse may be measured as use of drugs ever, according to time (e.g., in the past 30 days or year), or by frequency (e.g., has been drunk at least two times). From the latest HBSC survey of 11-15 year olds in 2012, it was estimated that for 11 year olds, 1% of girls and 3% of boys had been drunk at least twice (ever). Among 15 year olds, these rates were 43% and 38%. Only 15 year olds were asked about cannabis use: 24% of girls and 22% of boys had ever tried it, and 9% of both sexes had tried it in the last 30 days (29). From the latest Smoking, Drinking and Drug Use in England survey of 11-15 year olds in 2011 (35), it was estimated that 22% who drank any alcohol in the past four weeks, 54% of girls and 46% of boys had been drunk (i.e., 11.8% and 10.1% of all surveyed). In the same survey, it was estimated that in the past year, ~8% had taken cannabis, ~4% had taken volatile substances, such as sniffed glue, and ~1% had inhaled poppers.

HBSC = Health Behaviours in School Children

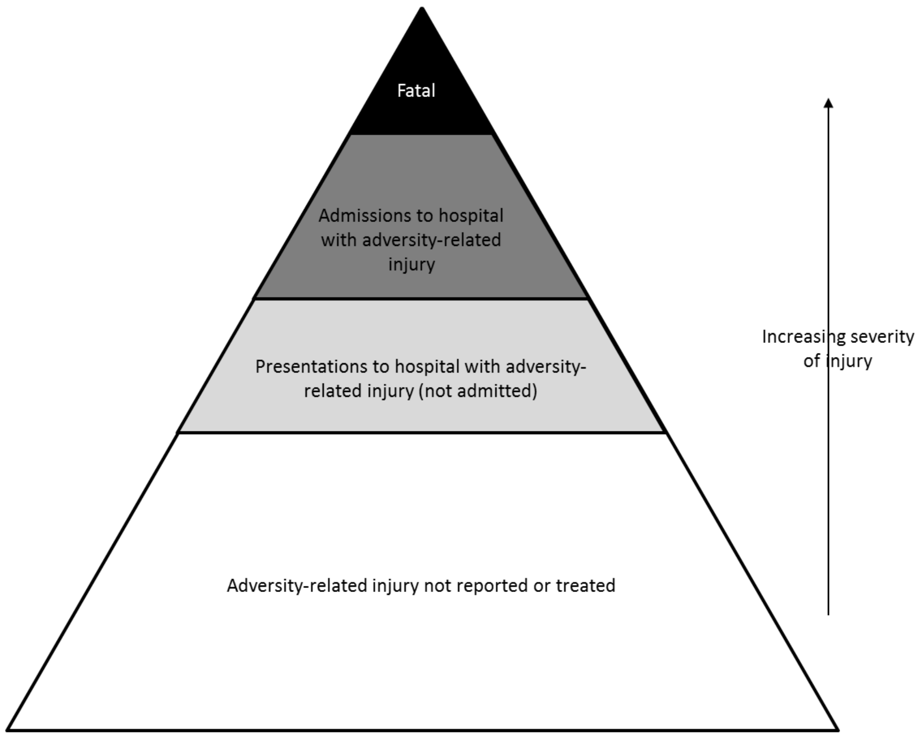
Case-definitions of **injury** can differ according to the research in question (36-39), and depend on both cause and pathology (40). For example, if the research is on injury that inflicts substantial cost on health services, the definition of injury may include ‘psychological injury’ (e.g., through neglect and abandonment), or ‘chronic injury’ (e.g., through occupational overuse syndrome) (36). In this thesis, I define injury as acute physical injury that carries a significant threat of pain, disability or death (e.g., a fracture or poisoning). Specifically, I consider any injury coupled with a record of violence as **violent injury**. ‘**Self-inflicted injury’** refers to all types of self-harm including self-poisoning (23, 24). **Drug/alcohol-related injury** refers to any injury coupled with any drug or alcohol use, including drinking within legal limits (41), because the combination of both alcohol and injury indicates a high likelihood of alcohol misuse (42, 43).

1.3.4 Why *emergency* presentations to hospital?

In Section 1.3.2 I described a healthcare contact as a 'teachable moment' (25), a phrase used in other areas of risk-taking behaviours, such as screening for HIV and smoking (44, 45). Such visits may present the opportunity for healthcare professionals to identify vulnerable adolescents, carry out assessments, and deliver interventions. Adversity-related injury that is severe enough to lead to a presentation to hospital may indicate a particularly high level of severity of injury or psychosocial need (25). Figure 1.4 shows increasing severity of injury as associated with an increasing likelihood of presentation to hospital (46). For example, clinicians are more likely to admit individuals who present with self-inflicted injury if they feel that he or she presents a high suicide risk (47).

This thesis focuses in particular on emergency (unplanned, non-elective) presentations to hospital. A presentation to hospital offers an opportunity to deliver assessment and intervention. Adolescents who present to hospital as an emergency may be more willing to accept help and engage with assessment and intervention due to the gravity of such an event for that individual (than they would be otherwise). This is supported by a cohort study of 10-15 year olds presenting with violent injury to an emergency department (ED; 'Accident & Emergency') in the United States (US). These adolescents were interviewed about their attitudes to their circumstances and possibilities of change. They had different perceptions about the preventability and likelihood of repeat violent injury when asked same questions two weeks later (25). Another cohort study of individuals (of all ages) who presented to an ED in England and who had misused alcohol found that the likelihood of keeping an appointment with an alcohol health worker was inversely related with the time between presentation and identification of alcohol misuse (26).

To conclude Section 1.3, adolescents who present to hospital as an emergency with adversity-related injury may have substantial underlying psychosocial need and risks of future harm, and could be targeted to reduce such risks. In the next section I review the research literature to determine the prevalence of such presentations among adolescents in England.



Based on a similar diagram in 'Violence and Injury. The facts.' WHO, 2012 (48)

Figure 1.4: Conceptual diagram of the severity of adversity-related injury and how these injuries present to healthcare services

1.4 Prevalence of presentations to hospital for adversity among adolescents in England

This section summarises what is currently known about the prevalence of emergency presentations for adversity-related injury, for adolescents in England, as a whole and by sex and age. I discuss cohort studies 1) of adolescents who have presented to hospitals in England with adversity in the past two decades (whether resulting in admission or not), and 2) that have employed population denominators to determine the prevalence of these presentations (or admissions).

1.4.1 What is known

I identified four relevant studies, which are summarised in Table 1.2. Three studies used National Health Service (NHS) admissions data for England (Hospital Episode Statistics or 'HES') to capture numbers of admissions for a single type of adversity-related injury (e.g., violent; the numerator). The fourth study captured numbers of admissions for self-inflicted injury in Oxford, through their own bespoke monitoring database of all hospitals in the region (49). All four studies used Office for National Statistics (ONS) population count data to derive denominator values.

Administrative hospital datasets (which were used for estimating prevalence in the four studies above) are unlikely to capture all adolescents who present or are admitted with adversity. For example, the clinician may not record alcohol misuse secondary to the presenting condition (this issue is discussed in further detail in Section 3.3.6). ONS population data (which were used to derive denominator values in the four studies above) acknowledge all nationally recorded births, deaths and migrations, and are assumed to be fairly accurate.

Therefore, it is likely that estimates discussed in this section provide lower limits for the true prevalence.

It can be seen from Table 1.2 that there are approximately 1) 25 to 200 hospital admissions in England for violence or drug/alcohol misuse per 100,000 adolescents (50, 51), 2) 67 to 1,423 presentations for self-inflicted injury per 100,000 adolescents per year (71% of these presentations followed by admission) (49), and 3) 125 to 325 admissions for self-inflicted injury per 100,000 adolescents (52). These estimates substantially vary by sociodemographic characteristics. For example, Figure 1.5 shows the estimated prevalence of emergency admissions for violent injury, by sex and year of age (from 0 to 75 years) from a published study by Bellis *et al* (51). Looking at the estimated prevalence at 10 to 19 years old, this was higher for boys than girls (note that the y-axis for graph A extends to 700 per 100,000 compared to that of graph B). The estimated prevalence of emergency admissions for violent injury was higher for patients from more socio-economically deprived areas (51). To my knowledge there are no published studies of the estimated prevalence of hospital contacts for violent or drug/alcohol-related *injury*.

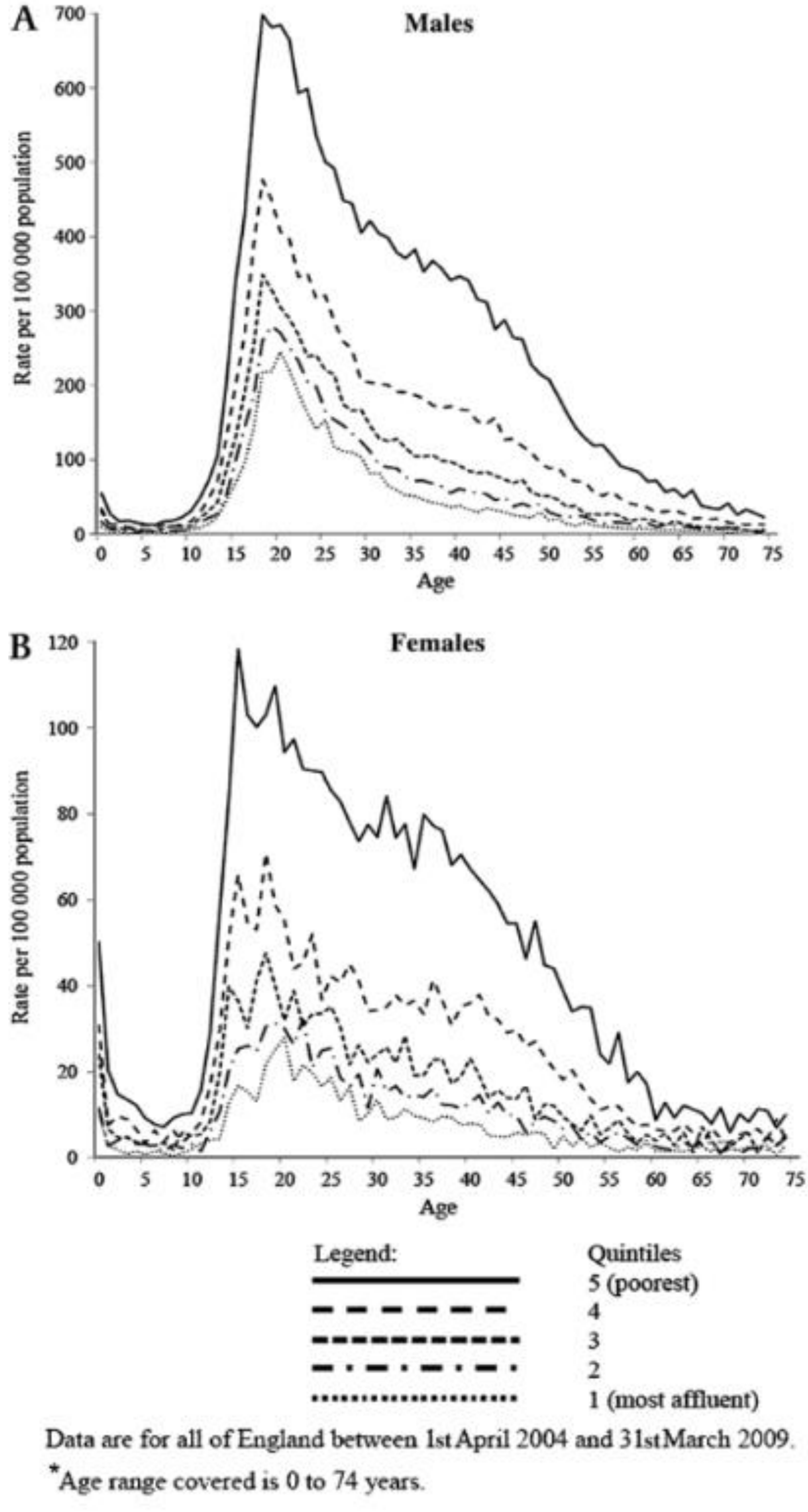
Table 1.2: Summary of studies reporting the prevalence of presentations for adversity among adolescents in England, 1995-2015

Study	Data source	Age (years)	Time period	Type of adversity, definition and whether with injury	Units	Prevalence*	Total numbers
Bellis *et al*, 2011 (51)	HES admissions data with ONS population denominators	0-75	Apr 2004-Mar 2009	ICD codes for direct physical violence	Emergency admissions	~25 to 200/100,000 10-19 year olds (varying by sex, age-year, and deprivation)	.
Wilkinson *et al*, 2002 (52)	HES admissions data with ONS population denominators	11-75	Apr 1995-Mar 2000	All ICD codes mentioning 'self-injury' or 'self-harm', except for 'personal history of self-harm'	Admissions	Approximately 125 to 325/100,000 10-24 year olds per year* (varying by sex, age-group and calendar year)	.
Hawton *et al*, 2012 (49)	MSSH database with ONS population denominators	10-18	Jan 2000-Dec 2007	Intentional self-poisoning or self-injury, irrespective of suicidal intent, collected through clinician forms and direct data entry.	ED presentations	67 to 1,423/100,000 10-18 year olds per year* (varying by sex and age-group)	7,150 presentations for 5,205 individuals
Chowdry *et al*, 2013 (50)	HES admissions data with ONS population denominators	12-19	Apr 1990-Mar 1999	20 ICD codes that mention 'drugs' or 'alcohol'**	Admissions	~0 to 150/100,000 12-19 year olds for drug misuse, 50 to 370/100,000 for alcohol misuse (varying by sex and age-year)	.

ED = Emergency department; HES = Hospital Episode Statistics; ICD = International Classification of Diseases; MSSH = Multicentre Study of Self-harm in England, ONS = Office for National Statistics

*Counting adolescents with one or more admissions only once (i.e., incident cases).

**International Classification for Disease codes, version 10: F10-F16, T40, X42, X45, X62, Y12, Y90, Y91, R780-R784. Elaine Kelly, Institute for Fiscal Studies (personal communication, 2013)



From Bellis *et al*, Injury Prevention 2011 (51). Reproduced with permission from the rights holder, *BMJ*.

Figure 1.5: Annual rates of emergency admissions to hospitals in England for violence (April 2004-March 2007) by sex, age*, and deprivation: (A) Males; (B) Females

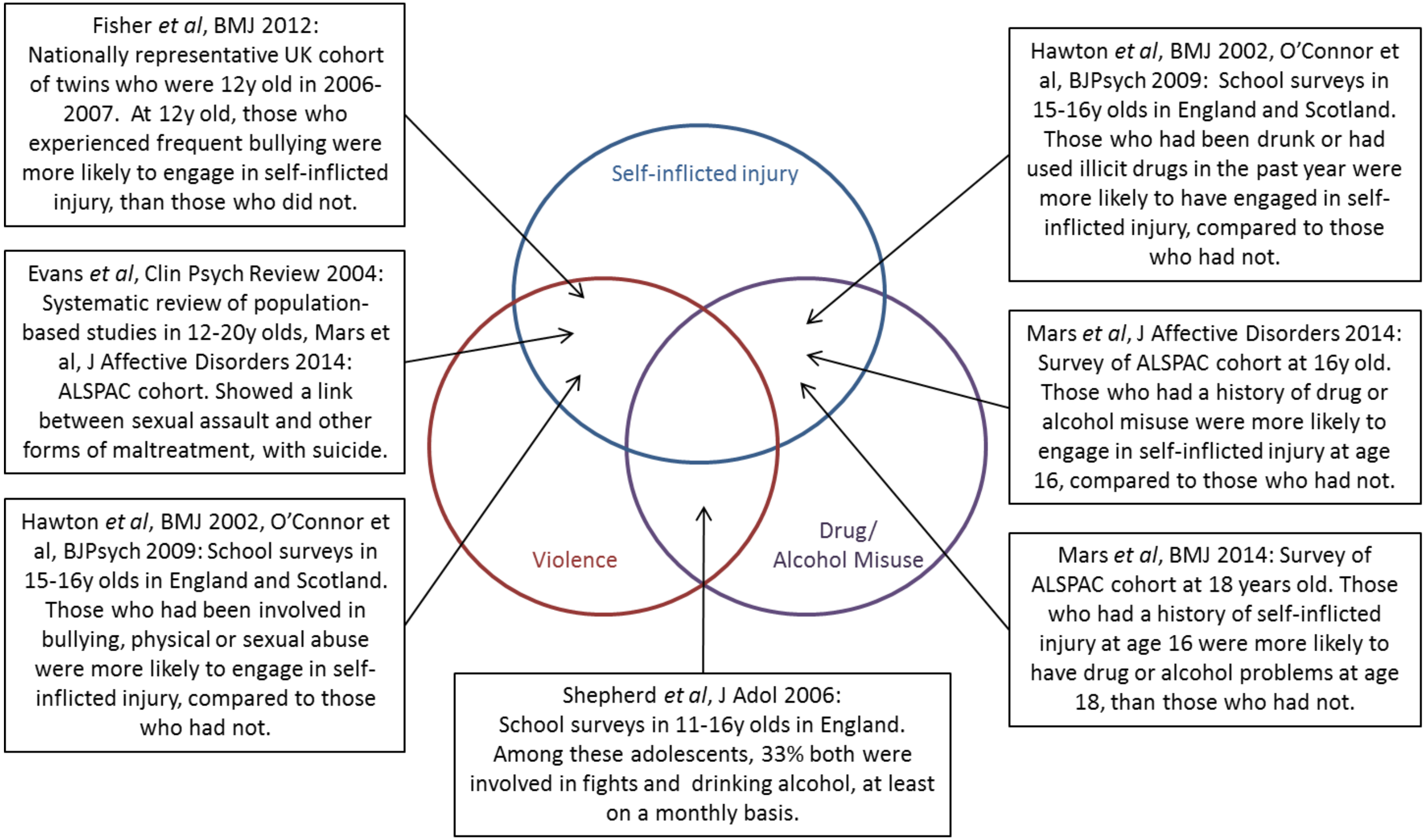
1.4.2 Gaps in the evidence

Adolescents may be exposed to more than one type of adversity at the same point in time or during the life-course. Several cross-sectional and cohort studies of adolescents from the general population, summarised in ALSPAC = Avon Longitudinal Study of Parents and Children

Figure 1.6, suggest that adolescents exposed to one type of adversity are likely to be exposed to other types during their adolescence. For example, Fisher *et al*'s cohort study of 12 year olds, representative of the UK general population, found that those who experience violence through bullying were also more likely to self-inflict injury (53). In addition, high rates of 'overlap' between different types of adversity-related injury have been shown for adolescents presenting to hospitals in the United States (US) (43, 54, 55). Based on this evidence from the US, and that on adults in the UK, the level of overlap between different types for adolescents presenting to hospitals in the UK could be substantial. For example, in the ongoing Multicentre Study of Self-Harm (MSSH), which collects data on all presentations of self-inflicted injury to hospitals in Oxford, Manchester, and Derby, Hawton *et al* reported that for adult patients (aged 18 years and over) admitted in 2000-2009, 36.1% had a history of alcohol misuse, and 58.4% of acts of self-inflicted injury had involved alcohol (which was associated with increased risks of repetition of self-inflicted injury) (56).

In the four reports in Table 1.2, the prevalence of a presentation or admission to hospital for more than one type of adversity was not reported. Therefore, it is difficult to know the true prevalence of presentations to hospitals in England for adversity as a whole. This would provide an estimate of the total burden on hospital services of adversity-related injury as a whole. Such an estimate would be impossible to derive from the four studies in Table 1.2 collectively, as they are from different time-periods to each other, and they do not report how many individual adolescents were admitted with other types of adversity-related injury. It could also inform us as to which adolescent sub-groups contribute the most burden. Wilkinson *et al* reported that, on average the numbers of patients admitted with self-inflicted injury accounted for over twice as many such admissions (Table 1.2) (52).

Another gap in the evidence is an accurate estimate of the prevalence of admissions for drug/alcohol misuse. Although I identified one study which estimated this prevalence among 12-19 year olds (Table 1.2) (50), these estimates were based on a narrow definition of drug/alcohol misuse (ICD codes of which are provided as a footnote to Table 1.2). There were 290 codes that mentioned drugs or alcohol but were not included to define drug/alcohol misuse in the study, and therefore it likely that the 'true' prevalence of drug/alcohol misuse in adolescents is in fact, far beyond the range of 0 to 350 per 100,000 that was estimated.



ALSPAC = Avon Longitudinal Study of Parents and Children

Figure 1.6: Evidence from UK-based studies for exposure to multiple types of adversity during adolescence (5, 25-30)

1.4.3 Implications for clinical guidelines

The level of overlap between different types of adversity-related injury for adolescents presenting to hospital in England have substantial implications for how these adolescents should be managed. Although a considerable proportion of adolescents who present to hospital with adversity-related injury may be exposed to multiple types of adversity, the way in which they are clinically managed substantially depends upon the presenting type of adversity-related injury (Table 1.3). For instance, NICE (National Institute for Healthcare and Clinical Excellence) guidelines for addressing psychosocial needs of patients who present to hospital with violent injury simply do not exist. Guidelines for short- and long-term management of patients presenting with self-inflicted injury mandate admission for those under 16 years old, and all patients require psychosocial assessment and consideration of referral to a psychological intervention such as cognitive behavioural therapy (CBT) (57, 58). In the case of drug and alcohol misuse guidelines focus principally on treating patients with dependence (59-64). They also recommend brief advice and consideration of motivational interviewing for 16-17 year olds presenting with alcohol misuse. Public Health England (PHE) guidelines for young people seen in the ED with alcohol misuse recommend to assess risk, advise, and refer, as illustrated in their suggested pathway (Figure 1.7). Evidence for a substantial overlap between certain types of adversity-related injury in adolescents who present to hospital would justify development of the guidelines to reflect the likelihood of co-occurring problems.

The next section reviews the evidence for the risks of future harm in adolescents who present or are admitted with adversity-related injury, and importantly, whether these risks differ according to the type of adversity-related injury.

Table 1.3: Summary of UK national clinical guidelines for management of adolescents presenting with adversity

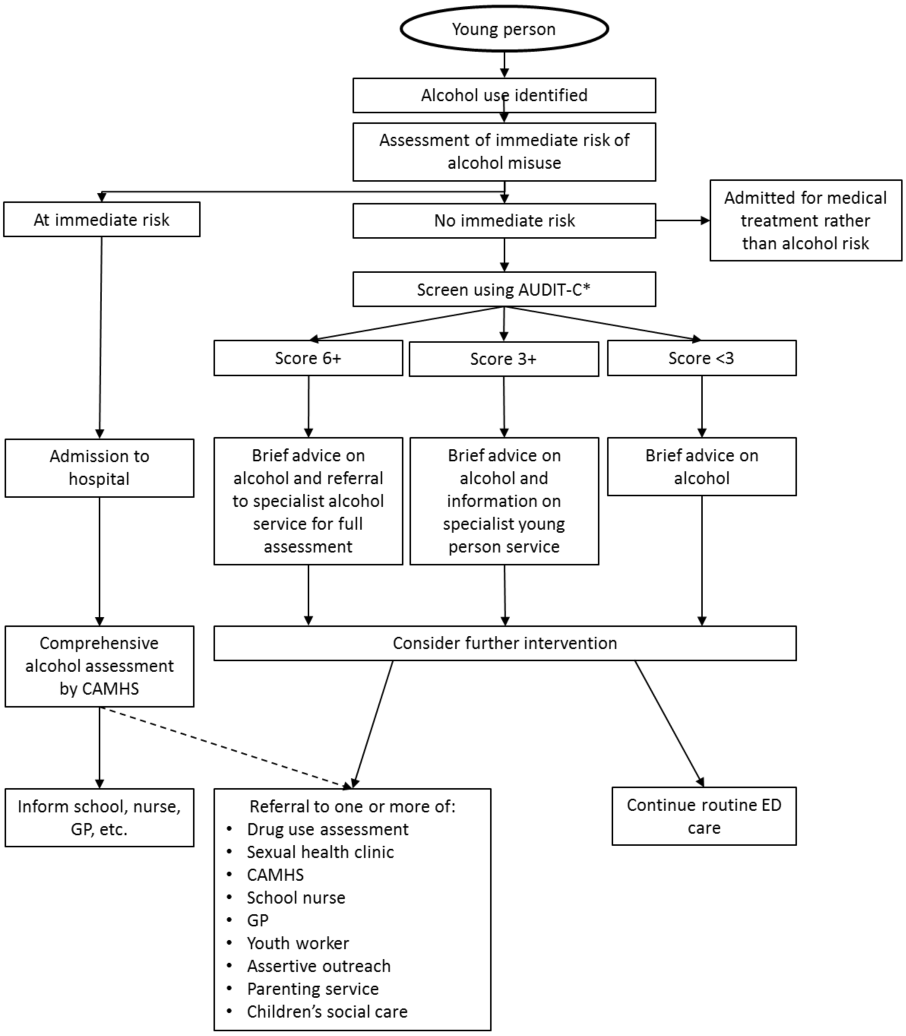
Type of adversity	Organisation, year	Type of adversity: Title	Key features
Violence	.	.	No guidelines available
Self-harm	NICE 2004 NICE, 2011	Self-harm: The short-term physical and psychological management and secondary prevention of self- harm in primary and secondary care (CG16)* Self-harm: longer-term management (CG133)	• Psychosocial assessment for all patients • Admission for all patients aged young than 16 years • Consideration of referral to a psychological intervention such as cognitive behavioural therapy
Drug/alcohol misuse	NICE, 2007 NICE, 2007 DH, 2007 NICE, 2010	Drug misuse: Opioid detoxification (CG52) Drug misuse: Psychosocial interventions (CG51) Drug misuse and dependence – guidelines on clinical management ('The Orange Book') Alcohol-use disorders: diagnosis and clinical management of physical complications (CG100)	• DH and NICE guidelines principally focus on recovery from addiction. • DH and NICE guidelines for drug misuse do not provide separate recommendations for adolescents or young people. • NICE guidelines for alcohol misuse recommendations: - 10-15 year olds: little evidence for effective interventions - 16-17 year olds: deliver brief advice and motivational interviews - 18-19 year olds: treated under the same recommendations as adults

(Table 1.3 continued)

Drug/alcohol misuse	NICE, 2010	Alcohol-use disorders: preventing the development of hazardous and harmful drinking (PH24)	• Alcohol Concern and PHE guidelines recommend that: - Alcohol-related attendances are strictly recorded - EDs have 'clear safeguarding thresholds with explicit courses of action' for young people - ED staff be trained in identifying alcohol-related presentations in young people, and be supported to deliver brief interventions, such as leaflets or short structured sessions of advice, to reduce harm • PHE support pack provides a flowchart of a model care pathway (see Figure 1.7).
	NICE, 2011	Alcohol-use disorders. diagnosis, assessment and management of harmful drinking and alcohol dependence (CG115)	
	Alcohol Concern, 2011	Reducing underage alcohol harm in Accident & Emergency settings	
	NICE, 2014	Alcohol use disorders overview ('NICE Pathways')	
	PHE, 2014	Young people's hospital alcohol pathways. Support pack for A&E departments	

CG = Clinical Guideline; DH = Department of Health; ED = Emergency department; NICE = National Institute for Clinical Excellence; PH = Public Health Guideline; PHE = Public Health England

*Recommendations about assessment of risk, children and young people, and interventions, were replaced with those within CG133 in 2011



Modified from 'Young people's hospital alcohol pathways. Support pack for A&E departments', PHE 2014 (65). Reproduced with permission from the rights holder, *Public Health England*. Dashed arrow is additional suggested action.
AUDIT-C = Alcohol Use Disorders Identification Test (-C indicates the 3-item version of the original 10-item AUDIT); CAMHS = Community Adolescent Mental Health Services; GP = General Practitioner

Figure 1.7: Model care pathway for adolescents who misuse alcohol and present to the emergency department, modified from Public Health England support pack (65)

1.5 Risks of future harm following a presentation to hospital for adversity: a systematic review

1.5.1 Introduction

Population-based cohort studies in several countries have shown that exposure to adversity during adolescence is associated with increased risks of poor physical health and poor psychosocial outcomes later in life such as injury, alcoholism, depression, poor educational attainment or low income, when compared to those not exposed (13-16, 66, 67). For example, for 49,411 18-20 year old male conscripts in Sweden surveyed in 1969-1970, those who responded that they had misused drugs or alcohol, or had contact with the police or juvenile services, were between 25% and 87% more likely to die from injury in the following 35 years (after adjustment for other risk factors for injury death), compared to those who responded that they had not engaged in these behaviours (68). Given that risks of harm are increased following exposure to adversity in the general population, it is likely that these risks are also increased following emergency admissions for adversity-related injury. To determine whether this was the case, I carried out a systematic review of the literature to find studies of risks of future harm, specifically in adolescents presenting to hospital with adversity-related injury. In this chapter I report on this systematic review.

I conducted a systematic search for studies reporting absolute or relative risks of any harm following adolescents' presentations to hospital (whether admitted or not), for any adversity (with or without injury).

Specific objectives of the review were to evaluate prognostic studies to:

1. determine absolute risks of harm, following presentations to hospital by adolescents for any type of adversity.

2. determine the relative risks of harm following a presentation for any type of adversity, compared with other presentations.

1.5.2 Methods

Inclusion criteria

I included journal articles published between January 1995 and January 2015 (inclusive), reporting results of cohort studies or randomised controlled trials (RCTs). I considered studies involving:

- adolescents, or groups of individuals where at least the majority were 10-19 years old (determined by the median [if not provided, mean] age, or proportions within age-groups)
- high-income countries, as defined by the WHO (24)
- presentations to hospital (whether admitted or not) with violence, self-harm or drug/alcohol misuse (with or without injury)
- longitudinally followed up for at least one month
- at least one recorded adverse physical or psychosocial outcome

Search and selection strategy

I searched PubMed for journal articles reporting on research studies, using terms provided in Appendix A.1. Studies were only considered if they were reported in either English or French. I removed any duplicates from my search, and then selected all articles where the study matched the inclusion criteria according to its title. I then reviewed the abstracts of the remaining articles, and removed any that clearly did not meet inclusion criteria (e.g., studies of adolescent populations not presenting to hospital). I reviewed the full text of the remaining articles, again removing any that did not meet inclusion criteria (e.g. articles where study outcomes were not reported separately for adolescents). Finally, I searched reference lists of the remaining articles for additional studies that might be eligible for inclusion.

Assessing risks of bias

Among studies that met the inclusion criteria, I assessed the risks of bias according to five domains, based on the Quality in Prognostic Studies (QUIPS) tool used by the Cochrane Prognosis Methods group (69, 70): study participation, study attrition, prognostic factor measurement, outcome measurement, and statistical analysis and reporting (described in Appendix A.2).

I rated each of the five domains (per study) as either contributing a low, moderate, or high bias (71). For studies where it was unclear what the levels of risk of bias was (e.g., if not enough information about the item was included in the report), these studies were defined as contributing ‘moderate’ bias for the domain in question.

For this systematic review I made some modifications to the original QUIPS tool to better correspond with the review’s objectives and inclusion criteria (these modifications and their justifications are described in Appendix A.2). For example, the original QUIPS tool contained a sixth domain: study confounding. I removed this domain for Objective 1 of the current review, which was to quantify the natural evolution of risk after discharge. That is, to quantify absolute risks of harm unadjusted for the effect of individual characteristics.

Reporting of results

I present absolute risks of outcomes stratified by any adversity-related, violent, self-inflicted, and drug/alcohol-related injury, respectively, and any combinations of different types of adversity-related injury (if reported). I present risks of each outcome separately (e.g., repeat injury, death). I also present risks of these outcomes within broader groups (e.g., any repeat self-inflicted injury that included repeat [non-suicidal] self-inflicted injury and repeat suicide attempts).

For risks reported at multiple time-points after discharge (e.g., at 3, 6 and 12 months), I present outcomes at each time-point. If different participants were followed for a range of times and one risk was estimated, I assumed this risk to be at the median follow-up time (mean if the median was not provided, mid-point of the range if neither mean nor median were provided). For one study in adolescents presenting with self-inflicted injury, outcomes were reported up to 6.9 years after discharge (72). However, absolute rates of these outcomes were not reported and so instead I present results from an earlier report of this study, on outcomes up to 5.5 years after discharge (73).

For studies that did not report confidence intervals (CIs) for estimates of risk (which was eventually the case for most studies in this review), I estimated 95% CIs of the risk estimate whilst assuming the standard error (SE) to be:

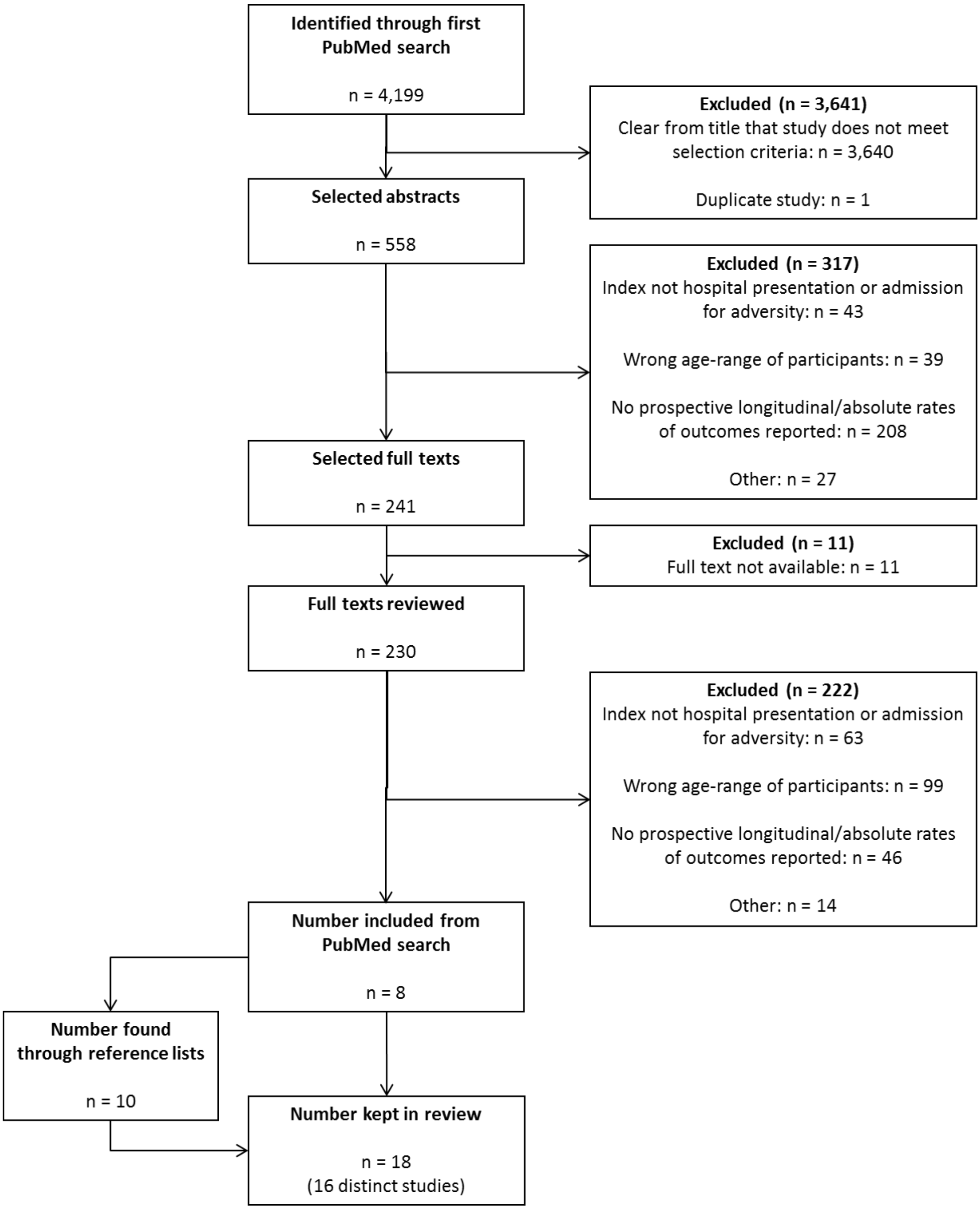
$$SE = \{estimate \times (1 - estimate)/Number\ of\ individuals\ at\ baseline\}^{1/2} \qquad [1]$$

that is, I used the equation for estimating the SE of a Binomial proportion (74). The estimate itself was based on estimates reported after potential attrition, at follow-up.

Most studies did not report risks separately by sex. For each study where risks of outcome were reported for each sex (75, 76), I present the risk that was the smallest between the two. I considered this smallest risk to be a conservative estimate of risk for the two sexes combined.

1.5.3 Results

The flow diagram in Figure 1.8 shows that the search retrieved 4,199 articles. After excluding articles not meeting inclusion criteria either through the article's title or abstract, there remained 241. Of these articles, 11 could not be retrieved through the UCL Library Service (references of which are provided in Appendix A.3). After reviewing the full texts of the remaining 230 articles, and searching relevant reference lists of the eight eligible articles (which retrieved ten additional eligible articles (55, 73, 75-82)), I included 18 articles reporting on 16 distinct studies in the current review.



Exclusion criteria: (1) studied only groups of individuals where the majority not 10-19 years old; (2) not from high-income countries; (3) did not include presentations to hospital (whether admitted or not) with violence, self-harm or drug/alcohol misuse (with or without injury); (4) participants not longitudinally followed up for at least one month; (5) did not include at least one recorded adverse physical or psychosocial outcome

Figure 1.8: Flowchart of articles in systematic search for reports of risks of harm following a presentation to hospital for adversity

Types of studies and participants

The 18 articles included in the current review comprise 16 studies (13 cohort studies and 3 RCTs) (Table 1.4) (55, 73, 75-91). Over half of the 18 articles reporting on these studies were published in the last decade (from 2006 onwards; n=10) (55, 75, 78, 81, 82, 84, 86, 87, 90, 91). Of the 16 included studies, half were in adolescents who were specifically admitted (n=8) (73, 77-80, 85, 88, 89). Of the 16 studies, there were 2 specifically in adolescents who presented to the ED with violent injury (84, 87); 12 of adolescents who presented with self-inflicted injury (73, 75-82, 85, 88-90), and 2 of adolescents who presented with injuries related both to violence and drug/alcohol use (55, 91).

All studies in adolescents presenting with violent and/or drug/alcohol-related injury were in patients from hospitals in the US (Table 1.4). All studies of adolescents presenting with self-inflicted injury were carried out in the US, UK or other European countries. Studies of adolescents with violent injury mostly involved males and older adolescents (15 years old upwards), who were predominantly African-American or Latino, and of low socio-economic status (Table 1.4). Studies of adolescents with self-inflicted injury were predominantly in females who were around 15 years old or slightly older, with around 60% being from a deprived background.

Table 1.4: Characteristics of studies included in the systematic review of risks of harm following a presentation to hospital for adversity

Type of adversity First author, year	**Country, years**	**Inclusion criteria**	**N**	**Male, (%)**	**Mean age, range (years)**	**Ethnicity**	**Socio-economic status**
Violence							
Downey 2007 (84)	US*, prior to 2004**	Presented to ED with violent injury***	84	50	19, 10-24	93% African-American or Hispanic	Not reported. 52% were high-school graduates
Wiebe 2011 (87)	US*, 2007-2008	Presented to ED with violent injury	42	63	15, 12-19	88% African-American	Not reported. 77% had ever been suspended from school, and 65.3% had mostly A, B or C grades at school
Self-inflicted injury							
Cassidy 2009 (75)	Ireland, 2000-2005	Presented to ED with self-inflicted injury	39	21	13, 8-15	Not reported	Not reported
Cotgrove 1995 (85)	UK, 1987-1990	Admitted after a suicide attempt (control group of RCT)	58	15	15, 12.2-16.7	Not reported	Not reported
Goldston 1999[†] (73)	US, 1991-1995.	Admitted after a suicide attempt	75	~49	~15, ~12-18	~80% White	~60% were in the 4^{th} and 5^{th} most deprived quintiles
Granboulan 1995 (77)	France, 1971-1980.	Admitted after a suicide attempt.	127	36	16, 12-22	Not reported	Not reported
Groholt 2006 & 2009 (78, 81)	Norway, 1992-1994	Admitted after suicide attempt	92	10	17, 11-19	Not reported	56% had parents in manual occupations or who were unemployed

(Table 1.4 continued)

Type of adversity First author, year	**Country, years**	**Inclusion criteria**	**N**	**Male, %**	**Mean age range (y)**	**Ethnicity**	**Socio-economic status**
Self-inflicted injury (continued)							
Harrington 1998 (88)	UK, prior to 1998**	Admitted‡ after self-poisoning and referred to CAMHS (control group of RCT)	77	10	15, 10-16	Not reported	64% were of 'manual social class'. 56% were from a family receiving benefits
Hawton 1999 (89)	UK, prior to 1999**	Admitted after self-poisoning	45	16	Not reported, 13-18	96% Caucasian	No reported
Hawton 2007 (82)	UK, 1978-1997	Presented to hospital after self-inflicted injury	2,839	42	Not reported, 15-19§§	Not reported	Not reported
Hawton 2012 (90)	UK, 2000-2010	Presented to hospital after self-inflicted injury	5,205	25	Not reported, 82% 15-18y, range: 7-18y	Not reported	Not reported
Hulten 2001 (76)	Italy, Finland, UK, Sweden, Norway, Germany, 1989-1995	Presented to hospital after suicide attempt	1,215§	28	Not reported, 15-19	Not reported	Not reported
Laurent 1998 (79)	France, 1988-1992	Admitted after suicide attempt	552	29	15, 8-17	Not reported	65% of adolescents had parents who regularly worked
Rotheram-Borus 2000 (80)	US, 1991-1994	Admitted after suicide attempt (control group of RCT)	75	0	15, 12-18	85% Hispanic/Latino	38% had a mother who was in full-time or part-time work

(Table 1.4 continued)

Type of adversity First author, year	**Country, years**	**Inclusion criteria**	**N**	**Male, %**	**Mean age range (y)**	**Ethnicity**	**Socio-economic status**
Violence and drug/alcohol misuse							
Cunningham 2015 (91)	US, 2009-2011	Presented to ED with drug misuse and/or aggression	599	59	20, 14-24	58% African-American	73% received public assistance
Walton 2010 & Cunningham 2012 (55, 86)	US, 2006-2009	Presented to ED with past year alcohol use and aggression (control group of RCT)	235	44	17, 14-18	56% African-American, ~39% White	57% received public assistance

ED = Emergency Department; RCT = Randomised Controlled Trial; * Country not given, but study team based in the US; ** No official follow-up, but so have based this year on when report published; ***The study report uses the phrase 'admitted to the ED', but the rest of the paper indicates that all patient who visited the ED were approached; †Also followed further to 6.9 years (72), but corresponding report does not give absolute rates of outcome; ‡The study report states that all adolescents who were referred to child mental health teams were approached. All four hospitals in the study had a policy of admitting children for an overnight stay if presenting with poisoning, so I have assumed all participants were admitted; §There were originally 1,264 individuals, but data on method of self-harm were missing for 51 of these individuals. The authors did not include these 51 individuals when they summarised outcomes of repeat self-harm; §§The original report was on 15-24 year olds, but only results for 15-19 year olds are presented here.

For the 16 studies, duration of follow-up after discharge from the index presentation, outcomes, and estimated risks are presented in detail in Appendix A.4. Table 1.5 summarises the duration of follow-up and outcomes studied. Few studies reported risks of outcomes other than repeat adversity (of the same type as at the index presentation, e.g., repeat violence following an initial presentation for violence). There was an exception for studies of adolescents presenting with self-inflicted injury. Some presented risks of death after discharge, for any reason (77, 78, 81, 90).

One study reported the increase in risks of an outcome following a presentation for adversity compared to these risks in the general population. In 15-24 year olds presenting to hospital with self-inflicted injury Hawton *et al* compared the risks of death over the 20 years after discharge, to expected risks of death for 15-24 year olds in the general population (82). The authors found that risks following a presentation for self-inflicted injury were ten times greater. No studies reported any risks of outcomes relative to adolescents presenting with a condition other than adversity (i.e., studies needed to address Objective 2 of this systematic review).

Table 1.5: Lengths of follow-up and types of outcomes, reported by studies included in systematic review of risks of harm following a presentation* to hospital for adversity

Outcome		**Type of adversity at index presentation***		
		Violent	**Self-inflicted**	**Drug/alcohol-related**
Within 1st year				
Same cause*:	Death	✓	✓	✗
	Repeat presentation**	✓	✓	✗
All cause:	Death	✗	✓	✗
	Repeat presentation**	✓	✓	▬
1-5 years				
Same cause*:	Death	✓	✓	✗
	Repeat presentation**	✓	✓	✗
All cause:	Death	✗	✓	▬
	Repeat presentation**	✗	✗	▬
5 years+				
Same cause*:	Death	✓	✓	✗
	Repeat presentation**	✓	✓	✗
All cause:	Death	✗	✓	▬
	Repeat presentation**	✗	✗	▬

✓ = Evidence available on risk of outcome after index presentation (by type of adversity); ✗ = no evidence; ▬ = partial evidence
*Or admission
**As at the index presentation/admission. For example, a repeat presentation to hospital for violence, following an initial presentation to hospital for violence.

Risks of bias

Table 1.6 summarises the judged levels of risks of bias according to the QUIPs tool, for studies included in the review (supports for these judgements are provided in Appendix A.5). A minority of studies included in the systematic review were considered to have low risks of bias in terms of study participation (25.0%), or study attrition (37.5%). Therefore, for the majority of studies, it was difficult to judge whether results of these studies may be validly extrapolated to this thesis's population of interest. Two studies, both in adolescents presenting to hospital in Europe with self-inflicted injury (78, 90), were judged to have low risks of bias in terms of study participation and attrition, but not in terms of prognostic factor measurement. In addition, a minority of studies were considered to have a low risk of bias in terms of outcome measurement (37.5%). These studies usually measured the explicit outcome death, from administrative hospital or mortality data.

Table 1.6: Brief summary of judged levels of risks of bias for each domain, for each study included in systematic review

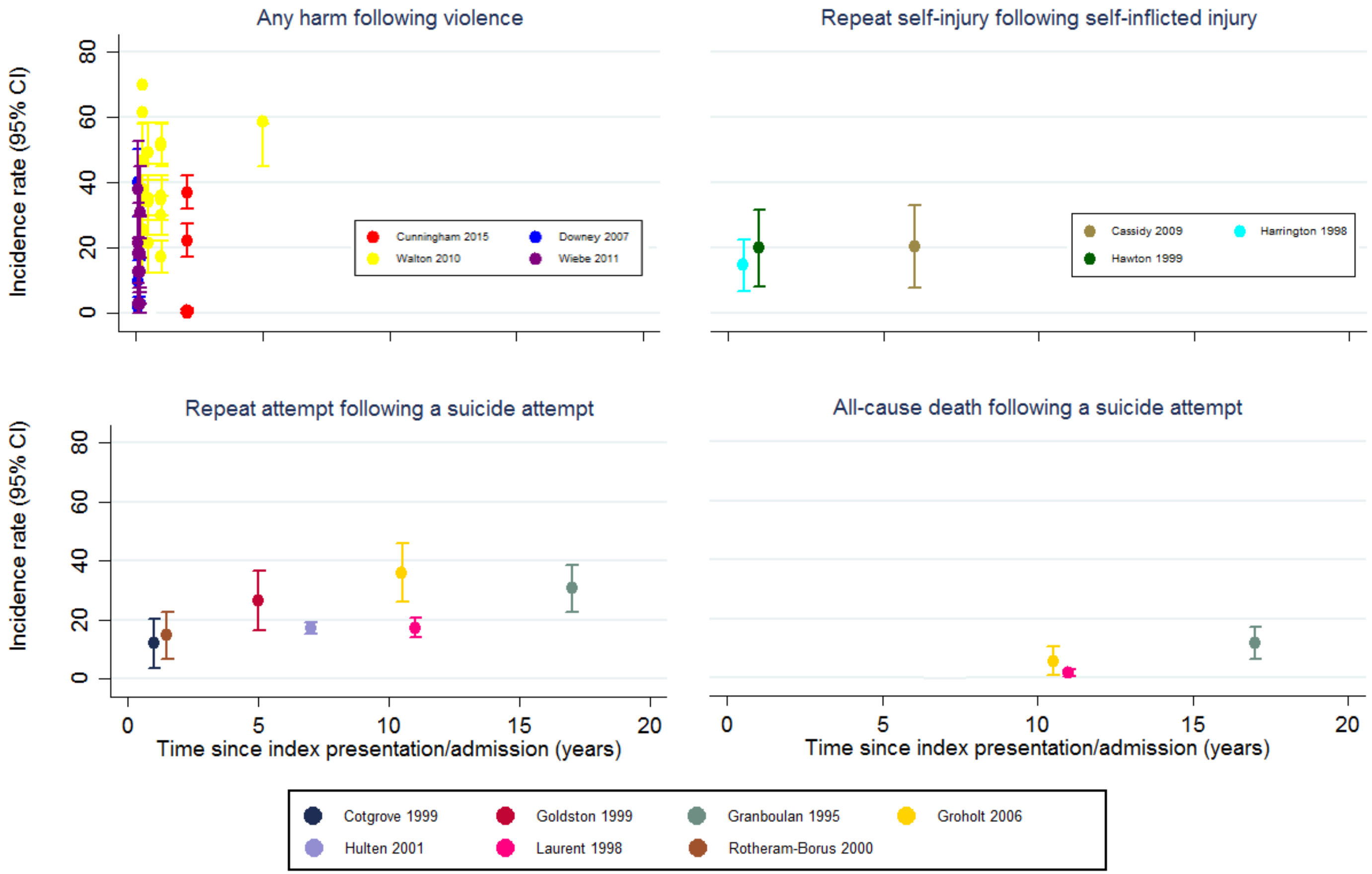
Study	Study participation	Study attrition	Prognostic factor measurement	Outcome measurement	Statistical analysis and reporting
Downey 2007 (84)	?	?	?	-	+
Wiebe 2011 (87)	?	?	+	?	+
Cassidy 2009 (75)	?	?	+	?	-
Cotgrove 1995 (85)	?	+	+	-	+
Goldston 1999[T] (73)	?	+	+	? and + *	+
Granboulan 1995 (77)	-	?	+	- and + **	-
Groholt 2006 (78)	+	+	?	? and + *	+
Harrington 1998 (88)	?	+	+	?	?
Hawton 1999 (89)	+	?	+	-	-
Hawton 2007 (82)	+	?	?	+	+
Hawton 2012 (90)	+	+	?	+	?
Hulten 2001 (76)	?	?	+	?	+
Laurent 1998 (79)	?	?	+	?	-
Rotheram-Borus 2000 (80)	?	?	+	-	-
Cunningham 2015 (91)	?	?	+	? and + ***	?
Walton 2010 (55)	?	+	+	-	+
% of applicable studies that are +	25.0%	37.5%	75.0%	12.5% to 37.5% [§]	52.9%

+, ? and - symbols indicate level of risk of bias for item: + = low, ? = moderate/unsure, - = high.
Justifications for above judgements provided in Appendix A.5.
* Moderate bias for repeat suicide attempts, low bias for death; ** High bias for repeat suicide attempts, low bias for death; *** Moderate bias for violent injury, low bias for death; § Depending on which judgements are used for Goldston 1999, Granboulan 1995, Groholt 2006, and Cunningham 2015.

Absolute risks of outcomes

Figure 1.9 is a broad summary of the estimated risks of harm after discharge, from studies included in the systematic review. Observed risks of outcomes during follow-up could be substantial, and varied greatly by index type of adversity and duration of follow-up. Following a presentation for violence, rates of further violence at one to six months ranged from at least 2.0% (threatening someone with a weapon) to 12.9% sustaining an injury requiring further medical attention, to 70.0% reporting violence consequences (Figure 1.9) (55, 84, 87). Risks of repeat violence were higher in adolescents presenting with violent and drug/alcohol-related injury compared to adolescents presenting with violent injury alone. By one year, 17.3% to 36.2% reported having misused alcohol and 30.0% to 50.2% reported having engaged in further violent behaviour (ranges given for different violent and alcohol outcomes) (86). Within the next two years, 37.2% returned to the ED with another violent injury (91), and 0.8% had died.

Following a presentation to hospital for self-inflicted injury, 17.3 to 20.0% of adolescents repeat self-harmed in the next seven years (Figure 1.9) (75, 90). Following a suicide attempt; up to 37.3% repeated an attempt within the next 17 years (73, 76-80), and 1.4 to 11.8% died. The majority of these deaths were either through suicide (33.1 to 50.0% of deaths) or accidental/unknown causes (38.6 to 60.2%).



Incidence rate per 100. Majority of CIs in figure estimated for the purpose of this systematic review and assumed to be based on incomplete data (see Section 1.5.2, 'Reporting of results').

Figure 1.9: Summary of reported risks of harm after discharge, for studies included in systematic review

1.5.4 Discussion

This systematic review retrieved 18 articles reporting on 16 cohort studies and RCTs in adolescents presenting to hospital with violence (sometimes coupled with drug/alcohol misuse) or self-inflicted injury. Up to 70.0% of adolescents with violence came to further harm in the following two years (varying by subtypes of harm, e.g., being threatened, beating someone up, etc.), and up to 36.1% with self-inflicted injury had a repeat self-inflicted injury in the next 17 years, with risks varying substantially according to length of follow-up. However, no studies reported risks following drug/alcohol-related injury unless coupled with violence (86, 91). Few studies reported risks of harm other than repeat adversity (e.g., risks of outcomes other than repeat violence, following a presentation for violence). Only one study compared risks of harm in adolescents presenting with adversity to those for other adolescents (i.e., risks of suicide following self-inflicted injury, compared to those in the general population) (82).

A strength of this review is that it included a broad range of research: I included studies where the majority of patients were 10-19 years old who presented with any adversity but not necessarily as an emergency or with injury, as well as (control groups of) RCTs. If I had included studies of only 10-19 year olds presenting as an emergency with adversity-related injury (the population of interest of this thesis), I would have included only five of the 17 studies in the current review, all of which were in adolescents with self-inflicted injury (73, 77-79, 89).

The main limitation of this review is that risks of bias of included studies were assessed only by myself. I concluded that none of the studies adequately addressed all domains of the QUIPs tool, and that it was likely that estimated risks of future harm following adversity in this review provided a lower limit for the ‘true’ risks. An additional reviewer may have made a less conservative conclusion. In addition, I did not search databases other than PubMed. Other databases could provide additional studies (e.g., Google Scholar), and I cannot definitively conclude that there exist no other reports of studies estimating risks of harm following drug/alcohol misuse, or comparing these risks to those in other populations. However, even if such a study does exist, it is unlikely that it would meet all of the gaps in evidence that have been identified in the current review (e.g., risks estimated at long-term follow-up, or of outcomes beyond repeat adversity).

It would be difficult to extrapolate the estimated risks following violent injury reported in this systematic review to adolescents hospitalised in England. The four studies in violent injury were conducted in the US, where cultures of violence and drinking behaviours and distribution of ethnic groups differ to that in the UK (Table 1.4) (92, 93). There is less difficulty in extrapolating estimated risks following self-inflicted injury in this systematic review to adolescents hospitalised in England, as all but one study were carried out in European countries (73, 75-79, 81, 82, 85, 88-90), and were principally in adolescents who were female, around 15 years old and relatively deprived, which corresponds to the highest rates of self-inflicted injury in the UK (8).

It is clear from this review that we have not yet established the full burden of future harm through any cause, for adolescents who present to hospital in England. As discussed in Section 1.4.2, such estimates could allow identification of particularly high-risk groups of adolescents with which to intervene. There is a need to determine whether these risks for different types of adversity-related injury are increased compared to following a presentation of admission for other reasons, which would indicate whether targeting interventions to adolescents with adversity-related injury could reduce their risks.

1.6 Effectiveness of psychosocial interventions for reducing future harm: an overview of systematic reviews

1.6.1 Introduction

The systematic review presented in Section 1.7 indicated that adolescents presenting to hospital with either violent or self-inflicted injury are at substantial risks of future harm over the next month to 20 years, but that little is known about risks following drug/alcohol-related injury or whether risks differ compared to other types of injury that are not adversity-related. Providing evidence of increased risks of harm for adolescents presenting or admitted with adversity-related injury may only be beneficial if there are proven effective interventions available to deliver.

In this section, I report an overview of systematic reviews. The aim of this overview was to determine the effectiveness of interventions for reducing risks of future harm. Its focus was on interventions that could feasibly be delivered in adolescents presenting to hospital in England with an adversity-related injury.

1.6.2 Methods

Search and selection strategy

I searched PubMed using terms that were synonymous for 'adolescent', 'violence', self-harm', 'drug', 'alcohol' (provided in Appendix B.1), alongside the terms 'review' or 'meta-analysis, for systematic reviews published between January 1995 and January 2015 (inclusive). I screened all articles retrieved from this search by title, then abstract, and finally by full text. After selecting full texts of reviews, I searched their reference lists. For any reviews that did not quite meet all inclusion criteria, I searched their reference lists for additional systematic reviews that would be eligible for inclusion. Finally, I searched the online clinical trials registers ISCRTN.com and ClincalTrials.gov for any eligible studies which were either ongoing or where the report was not yet published in PubMed. These latter studies are summarised in Appendix B.2 and the most relevant discussed in Section 1.6.4.

Inclusion and exclusion criteria for systematic reviews

I included reports of systematic reviews of interventions:

- to reduce risks of future harm
- delivered specifically to adolescents or young people (10-25 year olds)
- delivered following violence, self-harm or drug/alcohol misuse
- that could feasibly be initiated in hospitals in England
- evaluated using RCTs

I excluded any systematic reviews of:

- universal, school-based, GP-based or detention centre-based interventions
- interventions aimed at individuals who had already been referred for specialist substance abuse treatment

For any systematic reviews that included both RCTs and quasi-experimental studies, I included them in this current overview but did not include their overall findings. I included and discussed individual findings of only the corresponding RCTs.

Methodological quality of selected systematic reviews

For each selected systematic review, I assessed its quality according to 'A measurement tool to assess the methodological quality of systematic reviews' (the ASMSTAR tool) (Appendix B.3) (94), a checklist of 11 items concerning 1) a-priori design of the systematic review being stated in an ethics approval or study protocol, 2) number of study reviewers, 3) scope of the literature review, 4) inclusion of a grey literature search, 5) referencing of excluded studies, 6) description of individual study characteristics, 7) assessment of scientific quality of included studies, 8) consideration of scientific quality when concluding the results of the systematic review, 9) use of appropriate methods to synthesise results (e.g., meta-analyses), 10) assessment of the possibility for publication bias, and 11) description of potential for conflicts of interest for individual studies.

Reporting of results

I present the overall conclusions of each systematic review that met the above inclusion (and not exclusion) criteria, alongside the assessment of its methodological quality, grouped by type of adversity (most systematic reviews were of RCTs in adolescents with a specific type of adversity, e.g., violence).

In order to determine the effectiveness of an intervention across different types of adversity, I additionally present the results of the individual RCTs from these systematic reviews regardless of type of adversity and grouped by type of intervention. For each individual RCT, I summarise the general type of intervention (e.g., 'case-worker'), sample size and characteristics (e.g., age distribution), for how long participants were followed, which outcomes were measured, and the results at follow-up.

I do not present the results of any individuals RCTs where:

- results were published before 1995

- the majority of the group were not adolescents at the time of intervention (10-19 years old, determined by the median [if not provided, mean] age, or proportions of individuals within each age-group)
- interventions had been delivered to adolescents who did not present with adversity-related injury (e.g., adolescents that did not present with self-inflicted injury but were considered to be at high risk of suicide, as in Diamond *et al*, 2010 (95))
- outcomes measured did not relate to harm (e.g., compliance to treatment only, as in Spirito *et al*, 2002 (96))

Update of selected systematic reviews

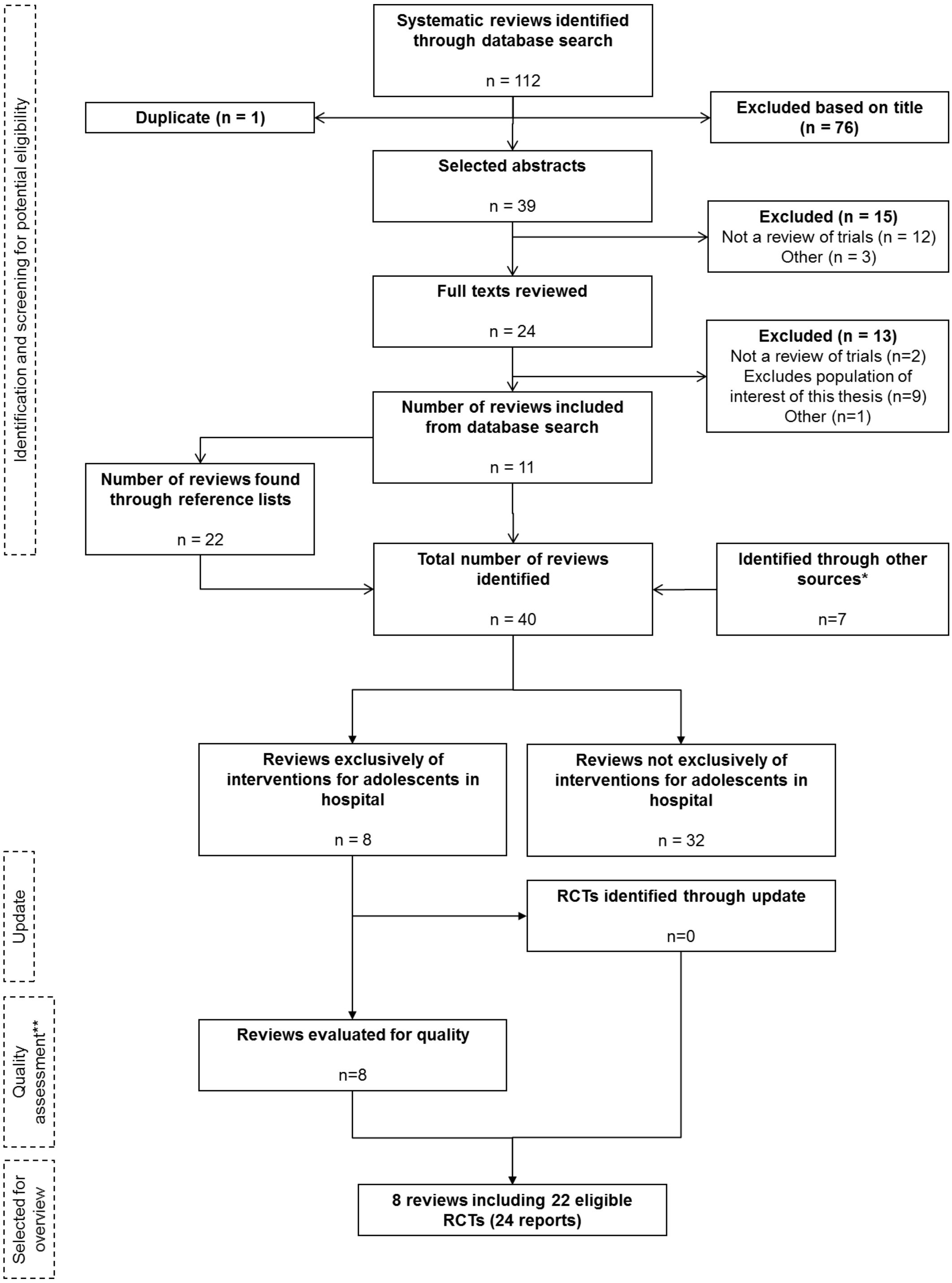
For each type of adversity-related injury, I attempted to update the most recent corresponding eligible systematic review. That is, I performed my own search in PubMed, which dated from when coverage of the search of the systematic review in question ended. For example, I found one systematic review of RCTs of interventions, for adolescents presenting with violence (97), which searched for RCTs published from 1980 to May 2006. Therefore, I searched in PubMed using terms that were synonymous for 'adolescent' 'violence' and 'intervention' (see Appendix B.1) for articles published between May 2006 and January 2015 (the time of writing), to identify any additional eligible RCTs (for each type of adversity-related injury, none were identified).

1.6.3 Results

Figure 1.10 is a flowchart showing that after the initial search of PubMed which retrieved 112 systematic reviews, and after review of titles, abstracts, full texts and reference lists, and some identification though other sources, I identified 40 potentially eligible systematic reviews of interventions to reduce harm following exposure to adversity. Among these 40, eight were exclusively of hospital-based interventions and evaluated in adolescents. These eight are included in this overview (the remaining 32 are presented in Appendix B.4) (98-105).

The literature searches of the eight included systematic reviews are summarised in Table 1.7. One systematic review was of interventions for adolescents presenting with violent injury (98), four for those presenting with self-inflicted injury (99, 102, 103, 105), and three for those presenting with drug/alcohol misuse (100, 101, 104). Three of the eight reviews included quasi-experimental studies as well as RCTs (98, 102, 105).

An additional six eligible trials were identified through searching ISCTN.com (n=1) and ClincalTrials.gov (n=5) registries (106-111). These trials are summarised as a table in Appendix B.2. One additional New Zealand –based trial was identified through colleagues (112). Some of these trials (those most relevant to the current overview) are discussed in Section 1.6.4.



*Principally through colleagues and other collaborators in my research term, and searching online profiles of research teams known to work in this area; **Assessed with the AMSTAR tool (Appendix B.3); RCT = Randomised Controlled Trial

Figure 1.10: Selection of systematic reviews and RCTs for overview

Table 1.7: Search characteristics of systematic reviews included in overview

Lead author, year	Scope of review	Time period that review covered	Databases searched	Number of studies retrieved
Population of interest: Adolescents presenting with violence				
Snider 2009* (98)	Hospital-based interventions for preventing youth violence.	Not reported. Submitted 24th Oct, 2007.	ACP Journal Club, CENTRAL, CINAHL, Cochrane Database of Systematic Reviews, DARE, EMBASE, MEDLINE and PubMed	7 articles for 4 distinct studies
Population of interest: Adolescents presenting with self-harm				
Burns 2005* (102)	Interventions targeting adolescents and young adults presenting to clinical services following self-injury or suicidal ideation	Not reported. Submitted 19th Sept 2004	CINHAL, Cochrane Database of Systematic Reviews and the Cochrane Controlled Trials Register, EMBASE, ERIC, MEDLINE, PsychINFO.	10
Newton 2010* (105)	ED-initiated intervention for improving health outcomes following suicide-related presentation among children	1985 to 2009	MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, EMBASE, Cochrane Central Register of Controlled Trials, HealthStar, Cochrane Database of Systematic Reviews, Health Technology Assessment Database, Database of Abstracts of Reviews of Effects, Academic Search Elite, PsycINFO, Health Source: Nursing and Academic Edition, CINAHL, SocIndex, ProQuest Theses and Dissertations, and Child Welfare Information Gateway, ClinicalTrials.gov, Reference lists, key journals, and conference proceedings (Canadian Association of Emergency Physicians, Society for Academic Emergency Medicine, American College of Emergency Physicians, Canadian Paediatric Society)	10
Robinson 2011 (103)	Interventions for adolescents and young adults presenting to a clinical setting with self-injury	1980 to June 2010	CENTRAL, EMBASE, Medline, PsycINFO	15, and 6 ongoing at the time of publication
Ougrin 2012 (99)	Interventions for reducing self-harm repetition in adolescents presenting with self-harm	Until Dec 2010	EMBASE, Medline, PsychINFO, and PubMed	14

(Table 1.7 continued)

Population of interest: Adolescents presenting with drug/alcohol misuse				
Kohler 2015 (104)	BMIs for young people who were admitted to an emergency care unit with indicators of alcohol misuse	Until 24th Sept 2013	CINAHL, Embase, Medline, PsychARTICLES, PsychINFO, PSYNDEX, Scopus	8 articles for 6 distinct studies
Newton 2013 (100)	ED-based BIs for reducing harmful and hazardous alcohol and other drug use and associated morbidities in youth.	1985-Apr 2011	Child Welfare Information Gateway, CINAHL, Cochrane Central Register of Controlled Trials, Cochrane Database of Abstracts of Reviews of Effects, ACP Journal Club, Database of Systematic Reviews, EMBASE, Health Technology Assessment Database, MEDLINE, OVID HealthStar, Ovid MEDLINE In-Process & Other Non-Indexed Citations, ProQuest Theses and Dissertations PsycINFO, SocIndex, ClinicalTrials.gov, "key journals (eg, Annals of Emergency Medicine, Pediatrics)", "conference proceedings (eg, Society for Academic Emergency Medicine, American College of Emergency Physicians)"	12 articles for 9 distinct studies
Yuma-Guerrero 2012 (101)	Screening, BI, referral to treatment for risky alcohol use among adolescent patients in acute care settings	Until Jan 2011	Google Scholar, PubMed, bibliographies of review articles and 'original research studies'.	7

***Included both RCTs and quasi-experimental studies**

A quality assessment of the eight selected systematic reviews is provided in Table 1.8. Most of the systematic reviews adequately met the majority of domains (i.e. presented low risk of bias). Most considered carrying out a meta-analysis of results (most could not actually do this because of too few, or heterogeneity between, eligible studies). However, only half of the eight systematic reviews described the studies that were excluded from the systematic review after reading the associated full text (n=4), and few considered the possibility of publication bias (n=2). One systematic review in particular, Yuma-Guerrero *et al* (2012), did not meet criteria for 10 of the 11 domains.

Table 1.8: Quality assessment of systematic reviews included in overview

Study	A priori design?	Duplicate selection/extraction?	Comprehensive literature search?	Grey literature search?	List of excluded studies provided?	Characteristics of studies provided?	Quality assessed?	Quality features in conclusions?	Methods to combine studies appropriate?	Likelihood of publication bias assessed?	Conflict of interest included?
Snider 2009 (98)	✗	✓	✗	✗	✓	✓	✗	✗	✓	✗	✗
Burns 2005 (102)	✓	✗	✓	✓	✓	✓	✗	✗	✓	✓	✗
Newton 2010 (105)	✗	✓	✓	✓	✓	✓	✓	✓	✓	✗	✗
Robinson 2011 (103)	✗	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗
Ougrin 2012 (99)	✗	✓	✓	✓	✓	✓	✓	✗	✗	✗	✗
Kohler 2015 (104)	✗	✗	✓	✗	✗	✓	✓	✓	✓	✓	✗
Newton 2013 (100)	✗	✓	✓	✓	✗	✓	✓	✓	✓	✗	✗
Yuma-Guerrero 2012 (101)	✗	✓	✗	✗	✗	✗	✗	✗	✗	✗	✗

Table 1.9 summarises the overall conclusions of the selected systematic reviews. Among the five systematic reviews that were exclusively of RCTs (99-101, 103, 104), two concluded that one or more interventions had shown effectiveness for reducing future harm following adversity (Table 1.9) (99, 104). Definitions of interventions that are discussed (e.g., Multi-Systematic Therapy) are provided in Table 1.10.

In Ougrin *et al*'s systematic review of interventions following self-inflicted injury, the authors concluded that **Multi-Systemic Therapy** (MST) was effective for reducing risks of repeat self-inflicted injury (99). However, both of the included RCTs that supported MST were in adolescents presenting with psychiatric diagnoses, but not necessarily self-inflicted injury (up to around half of the sample in each RCT had presented with self-inflicted injury) (113, 114). These are adolescents who would not meet criteria for discussion as individual RCTs in the current review. Ougrin *et al* also concluded that there was a lack of RCTs to confirm the effects of **Cognitive Behavioural Therapy** (CBT) and **Dialectical Behavioural Therapy** (DBT) (99).

Kohler *et al*'s systematic review of interventions following alcohol misuse concluded that **Brief Motivational Interventions** (BMIs) were at least as effective or more effective than other brief interventions (BIs), for reducing levels of alcohol consumption (104). Three of the five studies in Kohler *et al*'s systematic review revealed significant effects of BMIs for reducing levels of alcohol consumption (when compared to a control group) according to some measures of alcohol use but not others, within the same study (86, 115, 116). For example, Cunningham *et al* found that adolescents who received a BMI were less likely to report alcohol misuse (according to the AUDIT-C) or binge drinking at 3, 6 and 12 months later, compared to either standard care or a different BI (86). The authors also found that adolescents in the intervention group did not have significantly different AUDIT-C scores for drinking frequency or quantity.

Yuma-Guerrero *et al*'s systematic review concluded that screening, BIs, and referrals may be effective for reducing harm in adolescents presenting with alcohol misuse (101), but this systematic review also had the highest potential for risks of bias compared to the other seven selected systematic reviews.

Table 1.9: Results of systematic reviews included in overview

Lead author, year	Number of RCTs meeting inclusion and exclusion criteria for the current review: Author, year	Overall conclusion of systematic review or individual RCT findings
Population of interest: Adolescents presenting with violence		
Snider 2009* (98)	2: Cheng 2008, Zun 2004 & 2006	Individual RCT findings: Cheng *et al* found no significant differences in the effect of a case management programme compared to control in rates of repeat injury, weapon carrying or use of services at 6 months (117). However, this result may have been influenced by delayed enrolment and delivery of the intervention, as well as a high level of attrition. Zun *et al* found that adolescents who were part of a case management programme were more likely to use services (e.g., education, employment, mental health), and less likely to report repeat violence, within the first year following their initial violent injury, compared to controls (118, 119). However, the authors found no difference in attitudinal change. There was a high level of attrition in this study, along with the potential for measurement bias (different methods were used to ascertain service use, between groups).
Population of interest: Adolescents presenting with self-inflicted injury		
Burns 2005* (102)	2: Harrington 1998, Wood 2001	Individual RCT findings: Between the two eligible RCTs (there were three, but one was not in the population of interest of this thesis), group therapy was the only intervention trialled by RCT that showed a significant reduction in rates of repetition of self-inflicted injury at 7 months compared to the control group (120). The other RCT was of family problem-solving therapy sessions (88), which found no significant reduction in rates of repetition of self-inflicted injury at 2 or 6 months.
Newton 2010* (105)	1: Donaldson 2005	Individual RCT findings: Donaldson *et al* found no significant differences in the effect of one-to-one and family therapy sessions that were skills-based (e.g., problem-solving, affect management skills) on rates of suicide reattempt or ideation at 6 months (121).
Robinson 2011 (103)	8: Arsanow 2011, Cotgrove 1995, Donaldson 2005, Harrington 1998, Hazell 2009, King 2006, King 2009, Wood 2001	Overall conclusion: The reporting of conduct in these trials are poor and inconsistent. Only one study, of CBT, found a difference in outcome. Slee *et al* (not presented in the current overview as adolescents were identified at local mental health centres and not in hospital) (122), did not find a difference in the numbers of adolescents who self-harmed at 9 months, but did find a difference in the number of self-harm incidents overall.

(Table 1.9 continued)

Ougrin 2012 (99)	10: Arsanow 2011, Cotgrove 1995, Donaldson 2005, Green 2011, Harrington 1998, Hazell 2009, King 2006, King 2009, Ougrin 2011, Wood 2001	Overall conclusion: Dialectical behavioural therapy and CBT require RCTs to evaluate efficacy and effectiveness. Group psychotherapy was associated with a reduction in repeated self-harm (120), however this was not replicated in subsequent studies (123, 124). Multi-systemic therapy was associated with a reduction of suicidal attempts when compared with hospitalisation.
Population of interest: Adolescents presenting with drug/alcohol misuse		
Kohler 2015 (104)	4: Bernstein 2010, Cunningham 2012, Monti 1999, Spirito 2004, Walton 2010	Overall conclusion: BMIs appear at least as effective and possibly more effective than other BIs in the ED.
Newton 2013 (100)	9: Bernstein 2009 & 2010, Johnston 2002, Maio 2005, Monti 1999, Spirito 2004 & 2011, Tait 2004, Walton 2010	Overall conclusion: Clear benefits of ED-based BIs for reducing drug/alcohol misuse and associated injuries remain inconclusive because of variation in assessing outcomes and poor study quality.
Yuma-Guerrero 2012 (101)	6: Bernstein 2009, Johnston 2002, Maio 2005, Monti 1999, Spirito 2004, Walton 2010	Overall conclusion: It is unclear whether screening, BI or referral to treatment is effective for reducing risky alcohol use. Four of the seven studies showed significant effects but none reduced both alcohol consumption and related consequences.

*Included both RCTs and quasi-experimental studies. Individual RCT findings reported in table, rather than overall conclusion of systematic review.
CBT = Cognitive behavioural therapy; ED = Emergency Department; RCT = Randomised Controlled Trial

Table 1.10: Definitions of interventions discussed in overview of systematic reviews

Intervention	Definition
Brief Motivational Interventions (BMIs)	Typically a 20-40 minute dialogue initiated by a clinician or social worker with the adolescent, to discuss negative impacts of risk-taking behaviours and to set goals for the future (125). Other forms of BMIs could include a resource handout that contains leaflets about the effects of risk-taking behaviours, or a list of useful contact numbers (e.g., for social support).
Case-worker programme	Usually assignment of a social worker or volunteer mentor to support the individual with advice and referral to other services (111).
Cognitive Behavioural Therapy (CBT)	A form of psychotherapy based on problem-solving and challenging unhelpful thinking (99).
Dialectal Behavioural Therapy (DBT)	Combines elements of CBT and provision skills for coping in times for distress (99, 126).
Multi-Systematic Therapy (MST)	Assignment of a caseworker that takes into account multiple systems that the adolescent and family interact with (e.g., school, mental health teams, community activities), and is quite intensive (sometimes daily contact over a period of 3-6 months) (99).

Table 1.11 summarises the 22 RCTs of adolescents presenting to hospital with adversity, extracted from the eight systematic reviews (of a total of 46 RCTs). All of these RCTs generally took place in the time-period 1998-2005, mostly in the US, and evaluated the effectiveness (on reducing later harm) of either a 'case-worker' programme (127), therapy (cognitive behavioural, family, or group), a 'green card' (which allows re-admission to hospital on demand) (85), or some form of BMI. The median number of participants in these trials was 177 (range: 31 to 853). For most studies, adolescents were randomised to either one of the above interventions or a control group (a brochure of public services in the area or standard care), and followed up for six to 18 months.

Case-worker programmes were evaluated by RCT following each type of adversity-related injury (117, 119, 128-130), with heterogeneous findings (Table 1.11). For example, one RCT in adolescents presenting with violent injury reported a reduction in repeat violence at 12 months (8.1% of those in the case-worker group were involved in violence vs. 20.3% in the control group) (119), but not of repeat ED visits or arrests. Another found non-significant changes in incidence of repeat injury compared to the control group (117).

RCTs evaluating the effectiveness of therapies did so exclusively in adolescents with self-inflicted injuries (Table 1.11Table 1.11), and the majority found no significant changes in repeat self-harm (88, 120, 124) suicide attempts (121), or depression (80, 121, 128).

Some RCTs of BMIs were carried out in adolescents presenting or admitted to hospital with violent or drug-related injury, combined with alcohol misuse (Table 1.11), with mixed results. When Johnston *et al* evaluated the effect of delivering BMIs to adolescents admitted with any injury, they found no significant changes in drink driving, binge drinking, or weapon carrying, at 12 months compared to controls (131). Cunningham *et al* found that computer- and therapist-delivered BMIs for adolescents with both violent and drug/alcohol-related injury was associated with a reduction in reported alcohol-related consequences at all time-points (55, 86), but found no reduction in aggressive behaviours or drinking of alcohol at 3 or 6 months.

Table 1.11: RCTs extracted from systematic reviews that are included in overview

Case-worker programmes

Lead author, year	**Setting, years**	**Sample**	**N**	**Intensity of intervention**	**Control**	**Changes in outcome for intervention group (relative to control)**
Cheng 2008 (117)	US, 2001- 2004	10-15 year olds presenting to ED for violent injury	166	Counselling by telephone or in person for up to 4 months	Standard care	→Service use, repeat injury at 6 months
King 2006 (128)	US**, 1998-2000	12-17 year olds admitted after suicide attempt	289	Nominated peer or adult that provides information about emotional/behavioural disorders, treatments, suicide risks, and other resources, over 6 months	Standard care	→ Suicidal ideation/attempts, depression at 6 months
King 2009 (129)	US**, 2002-2005	13-17 year olds admitted after suicide attempt	448	Nominated adult provides information about emotional/behavioural disorders, treatments, suicide risks, and other resources, over 3 months	Standard care	→ Suicidal ideation/attempts, depression at 12 months
Tait 2004 (130)	Australia, prior to 2004	12-19 year olds presenting to ED with drug or alcohol misuse	127	Support person to facilitate attendance for substance abuse treatment. Duration of intervention not reported, but followed-up at 4 months.	Standard care	↑ Safe alcohol/drug consumption patterns → General Health Questionnaire scores, violence at 4 months
Zun 2006 (119)	US**, 1998-1999	10-24 year olds presenting to ED for violence	188	Meetings for assessment and referral to services over 6 months (starting at a weekly frequency, to bi-weekly, to monthly)	Brochure of community resources	↓ Repeat violence → Attitudinal change, repeat ED visits, arrests at 12 months

↑, ↓, →, other symbols, and abbreviations are explained below the entire of Table 1.11.

Therapy						
Lead author, year	**Setting, years**	**Sample**	**N**	**Intensity of intervention**	**Control**	**Changes in outcome for intervention group (relative to control)**
Asarnow 2011 (132)	US, 2003-2005	10-18y olds presenting to the ED for a suicide attempt or ideation	181	Brief youth and family therapy session (at the ED; length of session not reported) and motivational phone call within 48 hours later (and possibly 1, 2 or 4 weeks discharge)	Standard care and enhanced training for staff (level of training not reported)	→ Suicidal behaviour, severe depression, psychopathology at 2 months
Donaldson 2005 (121)	US, prior to 2005	12-17 year olds presenting to ED after suicide attempt	31	CBT sessions for adolescent (6 sessions) and parents (1 session), over 3 months	Standard care	→ Suicidal ideation or depression at 12 months
Green 2011 (123)	UK, 2002-2006	12-17 year olds referred to CAMHS after a presenting to hospital with self-harm	366	Developmental group therapy (a mean of 10 sessions)	Standard care	→ Repeat self-harm at 0-6 and 6-12 months
Harrington 1998 & Byford 1999 (88, 133)	UK, prior to 1998	10-16 year olds referred to CAMHS after presenting to hospital with self-poisoning	162	Home-based family therapy (4 home visits)	Standard care	→ Repeat self-harm at 6 months
Hazell 2009 (124)	Australia, prior to 2009	12-16 year olds referred to CAMHS after presenting to hospital with self-harm	68	Developmental group therapy (6 “acute” group sessions, followed by weekly group therapy in a “long-term group)	Standard care	→ Repeat self-harm at 6-12 months
Wood 2001 (120)	UK, prior to 2001	12-16 year olds referred to CAMHS after presenting to hospital with self-harm	63	Developmental group therapy (6 “acute” group sessions, followed by weekly group therapy in a “long-term” group)	Standard care	↓ Self-harm, use of standard care at 7 months

↑, ↓, →, other symbols, and abbreviations are explained below the entire of Table 1.11.

Brief Motivational Intervention						
Lead author, year	**Setting, years**	**Sample**	**N**	**Intensity of intervention**	**Control**	**Changes in outcome for intervention group (relative to control)**
Bernstein 2009 (134)	US, 2005-2007	14-21 year olds presenting to ED with drug misuse but not alcohol misuse	210	A 20 minute BMI and resource handouts (n=68)***	Two control groups: both received resource handouts, one group also assessed at 3 months	↓ Being high (among smokers) ↑ Abstinence, receiving referrals at 12 months
Bernstein 2010 (135)	US, 2004-2009	14-21 year olds presenting to ED with alcohol misuse	853	A 20-35 minute BMI and resources handouts	Two control groups: both received resource handouts, one group also assessed at 3 months	↑ Cutting back on drinking, abstinence, being careful about situations when drinking at 12 months
Johnston 2002 (131)	US 1999–2000	12-20 year olds presenting to ED with injury	629	A 20 minute BMI	Standard care	→ Driving after drinking, binge drinking, carrying a weapon at 6 months
Maio 2005 (136)	US, 1999-2001	14-18 year olds presenting to ED with minor injury.	655	Laptop-based interactive computer programme lasting about 30 minutes	Computer-based questionnaire (duration not reported).	→ Alcohol misuse scores, binge drinking at 12 months
Monti 1999 (115)	US**, prior to 1999	18-19 year olds presenting to ED with alcohol misuse	94	BMI lasting 35-40 minutes	Standard care and handout (lasting about 5 minutes)	↓ Alcohol-related injury, hospital admissions → Alcohol use at 6 months
Spirito 2004 (116)	US, prior to 2004	13-17 year olds presenting to ED with alcohol misuse	124	35-45 minute BMIs for both adolescent and family	Brief advice to stop drinking and handout	↓ Number of drinking days per month, frequency of high-volume drinking ↑ Alcohol-related injuries, drink driving → Quantity drunk per drinking occasion at 12 months

↑, ↓, →, other symbols, and abbreviations are explained below the entire of Table 1.11.

Brief Motivational Intervention (continued)						
Spirito 2011 (137)	US, 2003-2008	13-17 year olds presenting to ED with alcohol misuse	125	BMIs to for both adolescent (45 minute session) and family (1 hour video assessment task)	A 35-45 BMI for adolescent only	→ Number of drinking days per month, frequency of high-volume drinking, quantity drunk per drinking occasion at 12 months
Walton 2010, Cunningham 2012, Sharp 2015 (55, 86, 138) (three-arm RCT)	US, 2006-2009	14-18 year olds presenting to ED with violent injury and alcohol misuse	472	A 35 minute computer-delivered BMI	Brochure of community services	→ Severe peer aggression, experience of peer violence, violence consequences, alcohol misuse, binge drinking, alcohol consequences at 3 months ↓ Experience of peer violence, alcohol consequences → Severe peer aggression, violence consequences, alcohol misuse, binge drinking at 6 months → Severe peer aggression, peer victimization, violence consequences, alcohol misuse, binge drinking, alcohol consequences at 12 months

↑, ↓, →, other symbols, and abbreviations are explained below the entire of Table 1.11.

Brief Motivational Intervention (continued)						
Walton 2010 and Cunningham 2012 and Sharp 2015 (55, 86, 138) (three-arm RCT)	US, 2006-2009	14-18 year olds presenting to ED for violent injury.	489	A 35 minute therapist-assisted computerised BMI	Brochure of community resources	↓ Severe peer aggression ↓ Experience of peer violence ↓ Violence consequences → Alcohol misuse → Binge drinking → Alcohol consequences at 3 months → Severe peer aggression → Experience of peer violence → Violence consequences → Alcohol misuse → Binge drinking ↓ Alcohol consequences at 6 months ↓ Serious aggression towards peers ↓ Peer victimisation → Violence consequences → Alcohol misuse → Binge drinking ↓ Alcohol consequences at 12 months

↑, ↓, →, other symbols, and abbreviations are explained below the entire of Table 1.11.

Brief Motivational Intervention (continued)						
Walton 2010 and Cunningham 2012 and Sharp 2015 (55, 86, 138)	US, 2006-2009	14-18 year olds presenting to ED for violent injury.	489	A 35 minute therapist-assisted computerised BMI	Brochure of community resources	↓ Severe peer aggression ↓ Experience of peer violence ↓ Violence consequences → Alcohol misuse → Binge drinking → Alcohol consequences at 3 months → Severe peer aggression → Experience of peer violence → Violence consequences → Alcohol misuse → Binge drinking ↓ Alcohol consequences at 6 months ↓ Serious aggression towards peers ↓ Peer victimisation → Violence consequences → Alcohol misuse → Binge drinking ↓ Alcohol consequences at 12 months

↑, ↓, →, other symbols, and abbreviations are explained below the entire of Table 1.11.

Other						
Cotgrove 1995 (85)	UK, 1987-1990	12-17 year olds admitted after a suicide attempt	105	'Green card'***	Standard care	→ Suicide rates at 6 months

↑ and ↓ indicate a statistically significant larger increase and decrease (respectively) in rates of outcome (at the 5% level), for the intervention group compared to the control group; → indicates no statistically significant change in rates of outcome between the intervention and control groups; *Or admission; **The study location was not reported, but the study team was based in the US; ***'Green Card' = Token which allows re-admission to hospital on demand; ‡Numbers of participants are provided here in particular as groups were unbalanced. For all other RCTs described in this table, randomisation was 1:1; BMI = Brief Motivational Interview, CBT = Cognitive Behavioural Therapy, ED = Emergency Department

1.6.4 Discussion

This overview retrieved eight systematic reviews of interventions for reducing harm following presentations for adversity during adolescence, which included RCTs of case-worker programmes, therapies, and BMIs, studies of effectiveness following different types of adversity, separately, and outcomes at 6 to 18 months. These systematic reviews concluded that MST may be effective for reducing risks of repeat self-inflicted injury in adolescents at high risk of self-inflicted injury (rather than definitely presenting with such an injury), that BMIs may be effective for reducing risks of recurrent violence or alcohol misuse, and related consequences (104), and that RCTs are needed to establish the effects of CBT and DBT for adolescents presenting with self-inflicted injury. In addition, RCTs of case-worker programmes were identified across the eight systematic reviews, which had been evaluated following all three types of adversity-related injury. These RCTs reported evidence of effectiveness for reducing risks of repeat violence and alcohol misuse, for some outcomes but not others, and no evidence of effectiveness for reducing risks of repeat suicide attempts.

One strength of this overview of systematic reviews is that it was very inclusive. Though I only present the results of eight systematic reviews in the main report, those that were only just excluded were scrutinised for trials that these systematic reviews may not have captured (see Appendix B.4). This search revealed no extra RCTs that would have been eligible. I also searched through clinical trials registers and did not find any completed RCTs that would have been eligible. I did find three ongoing trials (65, 139, 140), which I describe later in this discussion. I evaluated the methodological quality of the eight systematic reviews using the AMSTAR tool to give different weights to their overall conclusions.

One limitation is that I cannot rule out that the published reports of some eligible RCTs were not captured. This overview did not aim to be exhaustive, but rather to capture the majority of RCTs. As the other 40 broader, and only just ineligible systematic reviews of interventions, did not capture any more RCTs (Appendix B.4), it is likely that this overview did capture the majority of eligible RCTs.

Reporting issues among the eight systematic reviews reduces the possible certainty about stated effectiveness of case-worker programmes, MST, and BMIs, and lack of RCTs for effectiveness of CBT and DBT. Ougrin *et* al's systematic review did not assess the potential for publication bias (Table 1.8) (99). Therefore Ougrin *et al* may have over-estimated the effect of MST or the lack of RCTs in CBT and DBT (due to lack of publication of negative results). Similarly, Kohler *et al*'s systematic review did not include a search of the grey literature (104). However, the authors' conclusions, of heterogeneous findings for effectiveness of BMIs following alcohol misuse, remained unchanged when supplemented in the current overview with additional RCTs evaluating BMIs following any injury or specifically violent injury. It is unlikely that additionally identified RCTs in the grey literature (that were also not registered as clinical trials), would be of sufficient size and methodological quality to alter this conclusion.

Current NICE guidelines for managing patients presenting with self-inflicted injury or alcohol misuse, both published in 2011, have based their recommendations for managing young people on internal reviews of the literature (57, 62). The corresponding review for self-inflicted injury included nearly all corresponding RCTs in the current overview (except the two non-UK RCTs) (128, 129). Based on these reviews, self-inflicted injury guidelines recommend a consideration of offering CBT, but its effectiveness for reducing the incidence of repeat self-inflicted injury clearly still needs to be confirmed. Guidelines for alcohol misuse recommend delivery of BMIs (Table 1.3) (62). These recommendations are based on effectiveness shown in educational settings, due to a lack of studies in an ED setting.

The current overview does little to supplement the self-inflicted injury guidelines, but the additional search of clinical trial registers did identify one relevant RCT that had just finished recruiting at the time of writing (140): this RCT evaluated the effect of delivering BMIs to adolescents admitted with self-inflicted injury to hospitals in Scotland, the first to evaluate BMIs following this sub-type of adversity. The current overview also provides further evidence that BMIs may be effective for reducing harm for adolescents who present to hospital with alcohol misuse. Currently in progress, the 'SIPS Junior' and 'Quickfix' RCTs (112, 139), which will evaluate the effect of BIs for different age-groups of adolescents presenting to UK-based EDs with alcohol-related problems, may provide a more definitive conclusion.

Finally, this overview raises the question of whether case-worker programmes should be further evaluated in a UK-based population, in adolescents presenting or admitted to hospital with any adversity-related injury. This overview retrieved two US-based RCTs reporting potential effectiveness (119, 130), but violence and drinking cultures, as well as the health system, are very different for adolescents in the UK.

Evidence of increased long-term risks of harm for adolescents who present or are admitted with adversity-related injury (compared to other presenting or admitted adolescents), would justify large trials of case-worker programmes in adolescents admitted with *any* adversity-related injury. Exploratory work in these adolescents, for example, that identifies different risks in demographic and clinical sub-groups, could be used to inform the design of such trials.

1.7 Conclusions of Chapter 1

This chapter has demonstrated that adolescents are a vulnerable population, and that violence, self-harm, drug or alcohol misuse, and associated mortality and morbidity, affect a substantial proportion of this population. Adolescents who are exposed to adversity to such a degree that they present to hospital (or are admitted) as an emergency, with injury, may not only allow identification of some of the most extreme cases of vulnerability, but also provide a 'teachable moment', with which to intervene and engage with these adolescents.

Until now, recommendations for managing adolescents seen in hospital with adversity-related injury have varied between different types of adversity-related injury, despite the fact that these same adolescents may present with different types on different occasions. Evidence for this 'overlap' between different types of adversity-related injury, and for an increased risk of future harm, could inform the development of national clinical guidelines and research into interventions to reduce risks of future harm in this population.

There is a lack of evidence on the risks of future harm following adversity-related injury, particularly beyond the first year and for all-cause outcomes. Estimated risks of any harm following adversity-related injury, according to different demographic and clinical factors, could indicate which sub-groups of adolescents might stand to benefit most from an effective intervention. Evidence of increased risks of harm following adversity-related injury, compared to adolescents presenting or admitted to hospital for other reasons, would strengthen the argument that these adolescents may benefit from intervention. This could also justify pilot work for a large RCT of interventions that have yet to be properly explored in the UK, such as case-worker programmes, or further development of existing therapies and BMIs.

Chapter 2 Thesis aim, objectives, hypotheses, and further chapters

The aim of this thesis was to:

Characterise the population of adolescents admitted to hospitals in England as an emergency for adversity-related injury, and to determine their risks of future harm.

I focus on *admissions* to hospital in particular for three reasons. First, an admission indicates that the severity of injury or psychosocial need may have passed a certain threshold (as discussed in 1.3.4). Second, admissions are likely to provide more opportunities to communicate with and assess the psychosocial needs of adolescents with adversity-related injury, compared to emergency presentations that do not result in admission. Third, national data on admissions since 1989 are available as Hospital Episode Statistics (HES) (these data are described in Chapter 3). National data for other presentations to hospital (emergency department and outpatient visits) do exist but have not been established for as long, and are known to have substantially lower levels of recording (141). Results and conclusions from analyses of admissions data in this thesis should still to some extent inform on the potential socio-demographic and clinical make-up of adolescents who present, and are not necessarily admitted.

Specific objectives were to:

1. *Estimate the prevalence of an emergency admission for adversity-related injury (overall and by type of adversity-related injury [violent, self-inflicted, drug/alcohol-related]), during adolescence (between 10*

and 19 years of age), by sex and other socio-demographic and clinical factors.

2. *Among adolescents admitted with adversity-related injury, determine the proportion admitted with multiple types of adversity-related injury, either at the same admission, or at multiple admissions during adolescence.*

3. *Estimate the absolute risks of death and emergency re-admission in the ten years after discharge from an emergency admission for adversity-related injury during adolescence.*

4. *Compare ten-year risks of death and emergency re-admission following adversity-related injury with those following accident-related injury.*

5. *Quantify ten-year cause-specific risks of death (homicide, suicide, drug/alcohol-related, accidental, other) following adversity-related injury, and compare these risks to those following accident-related injury.*

Hypotheses of this thesis were that:

- Among adolescents admitted with adversity-related injury, a substantial proportion of these adolescents would be admitted with more than one type of adversity-related injury.
- Risks of death and emergency re-admission would be increased after each type of adversity-related injury, compared with risks after accident-related injury.
- Adolescents admitted with adversity-related injury would be at increased risks of deaths related to causes other than the index adversity-related injury. For example, adolescents admitted with violent injury would be at increased risks of suicide.

In Chapter 3, I discuss the data sources which I used to address the above objectives. These datasets are HES linked to Office for National Statistics mortality data, and mid-year population estimates. In Chapter 4, I present results from analyses to address Objectives 1 and 2 (Study I). For addressing Objectives 3 to 6, I analysed time-to-event data, where the events were death and emergency re-admission. These data had a multi-level structure. For example, an adolescent could have more than one index emergency admission for adversity-related injury, at which to estimate risks of subsequent events. Chapter 5 presents time-to-event statistical methods that I considered for addressing Objectives 3 to 6, which took the within-subject correlations in multi-level data into account. In Chapter 6, I present results from analyses addressing Objectives 3 and 4 (Study II), and in Chapter 7 I present results from analyses addressing Objectives 5 and 6 (Study III). In Chapter 8, I discuss the impact of the findings of this thesis on current policy, practice and research.

All analyses in Studies I to III were carried out in Stata/SE 12 (StataCorp). Any venn diagrams were drawn using EulerAPE version 3. Remaining graphs were drawn using Stata/SE 12 and Microsoft Excel.

Chapter 3 Data sources

3.1 Chapter summary

This chapter describes the datasets used in this thesis: 1) Hospital Episode Statistics (HES) inpatient data linked to Office for National Statistics (ONS) mortality data, and 2) ONS mid-year population estimates. In Sections 3.3 and 3.4, I describe how each dataset is processed and how admissions on the same individual are deterministically linked by NHS Digital. Admissions for some individuals are less likely to link, and therefore rates of some outcomes such as re-admissions may be under-estimated.

In Section 3.3, I define the exposures, outcomes, and covariates for the three studies in this thesis, and describe how these were derived in HES-ONS data (e.g., the exposure of adversity-related injury was defined using clusters of International Classification of Diseases version 10 codes). In Section 3.4, I also describe the calculations I carried out in ONS mid-year population estimates to derive denominators for estimating population prevalence.

Throughout this chapter, I consider strengths and limitations of these data for meeting the objectives of this thesis. A principal strength was that these data captured the majority of the population of interest and were sufficiently large with which to study adolescent sub-groups (e.g., age-groups). An important limitation (alongside that of linkage error, described above) was that ICD-10 codes in HES-ONS data were likely to be only moderately sensitive for capturing adversity-related injury or deaths.

3.2 Introduction

This thesis aimed to characterise the population of adolescents admitted to hospitals in England as an emergency with adversity-related injury, and to describe their risks of future harm. I addressed this aim in three separate studies, described in Chapters 4, 6 and 7. The analyses of these studies used Hospital Episode Statistics (HES) for inpatients linked to Office for National Statistics (ONS) mortality data (or 'HES-ONS'), and ONS mid-year population estimates.

In Chapter 3 I provide a background to HES-ONS data and ONS mid-year population estimates, and their strengths and limitations for meeting the aims of this thesis. I describe how within these datasets I defined adolescent cohorts, the main exposure (adversity-related injury), the comparison group (accident-related injury), outcomes (numbers of admissions, emergency re-admissions, death), other covariates (e.g., ethnicity), and denominators for population prevalence.

3.3 Hospital Episode Statistics inpatient data linked to Office for National Statistics mortality data (HES-ONS)

3.3.1 Background

HES inpatient data (referred to in this thesis simply as 'HES') are collected on all National Health Service (NHS) hospital inpatient (admissions) activity in England (142). These data have been routinely collected since 1989, but it is only possible to link admissions for the same individual for 1997 onwards (143). HES data contain information about dates and hospital location of admissions (and discharges) within the NHS in England, and about related diagnoses, operations and procedures. The primary purpose of HES is to inform governmental bodies for making decisions about the management of healthcare resources (144). However, this role was extended in 2002, to pay hospitals according to the care they provide, a system known as 'Payment by Results' (PbR) (145).

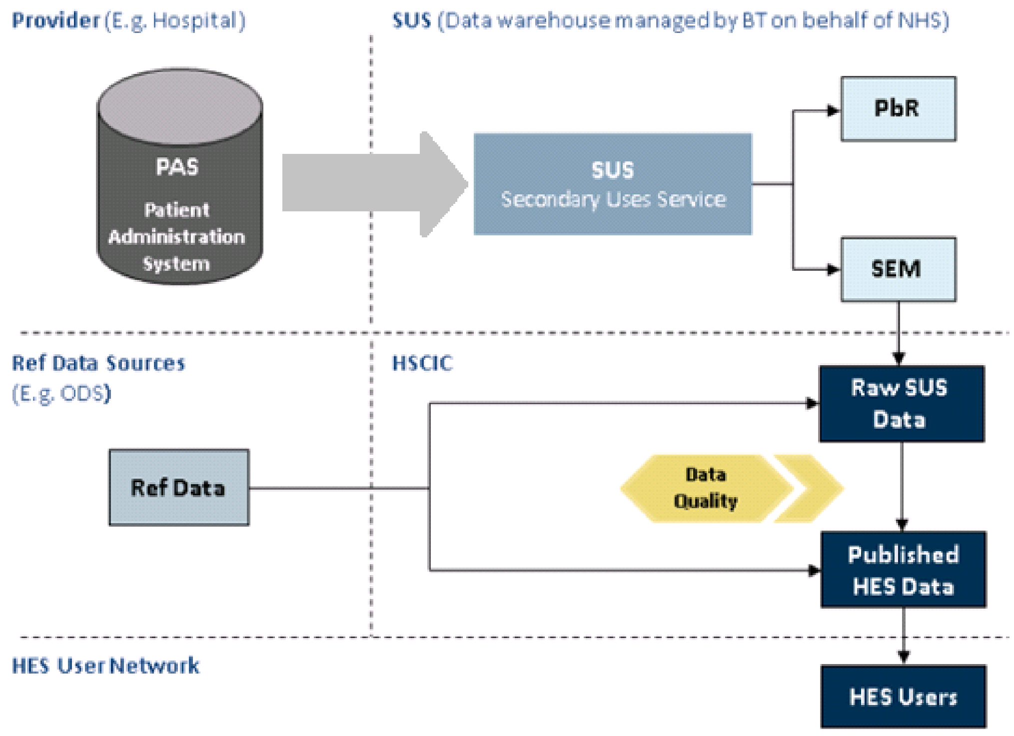
ONS mortality data contain information on dates, locations and perceived causes of death, for all deaths registered and certified in England and Wales (146). The ONS collect data on mortality in accordance with the Statistics Registration Service Act 2007 (147), for "informing the public about social and economic matters" and "assisting in the development and evaluation of public policy". The ONS send their mortality data to NHS Digital (previously the Health and Social Care Information Centre) on a monthly basis (148), which NHS Digital link to their latest extract of HES data.

3.3.2 Data processing and linkage

HES data are managed by NHS Digital since 2005 (previously managed by an executive body of the Department of Health). Figure 3.1 illustrates the routine process for generating HES data. Each record in HES first comes into existence when the clinician sees the patient and enters information about the visit in clinical records (via the Patient Administration System [PAS]).

Hospital-based coders enter information from clinical notes on to a computer system, in a standardised way as International Classification of Disease (ICD) codes. That is, if the same diagnosis is noted in different ways by different clinicians (e.g. 'maltreatment', 'maltreated child', 'poor treatment by parent'), it is entered on to the system under one standard ICD code. ICD codes are described further in Section 3.3.3, and implications of this coding in Section 3.3.6.

The standardised data are sent to the Secondary Uses Service who submit them to NHS Digital (as well as the PbR team). NHS Digital clean, quality check, and pseudonymise (pseudo-anonymise) the data before making them available to HES Users, including researchers (149).

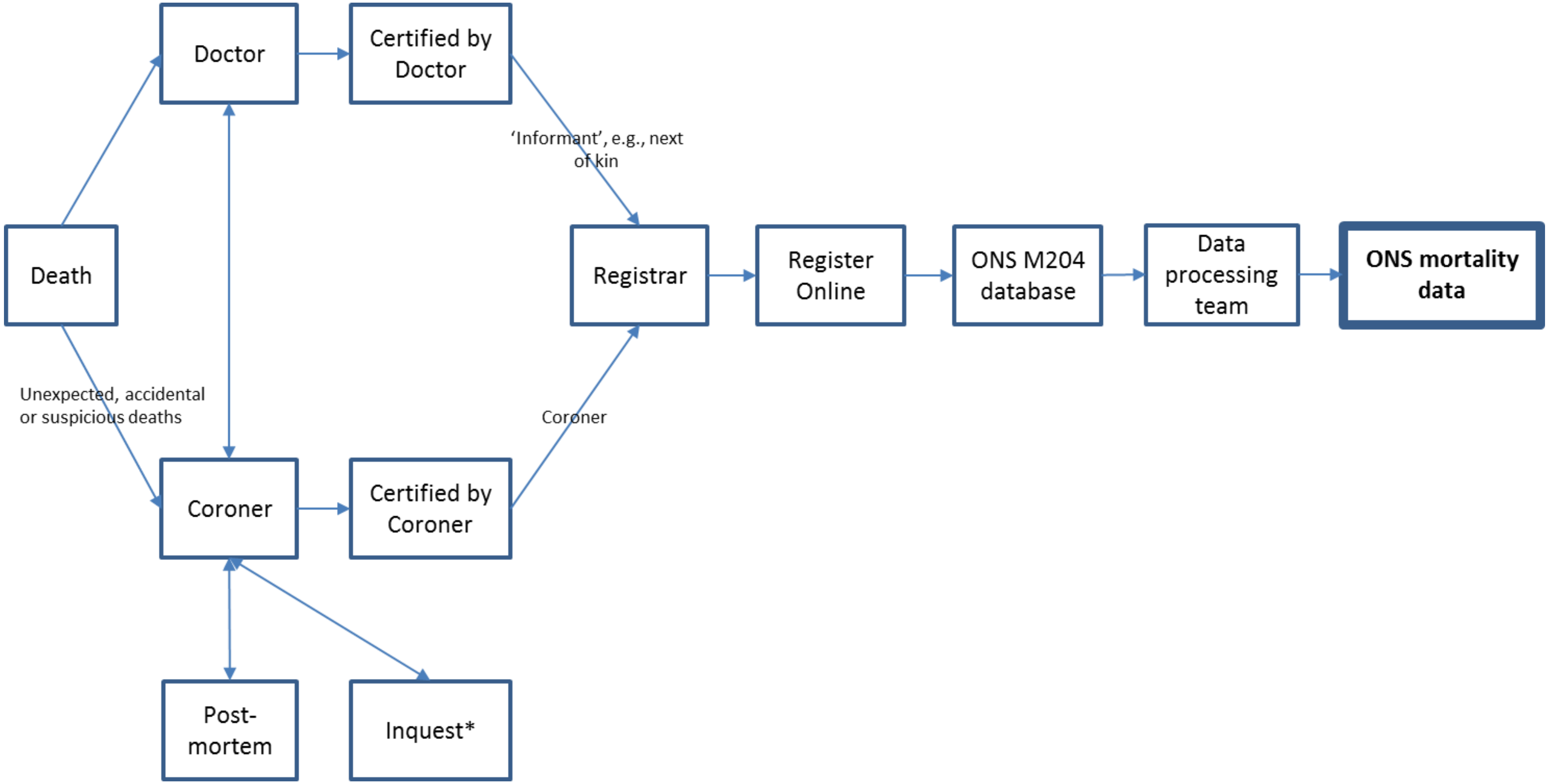


BT = British Telecom, HES = Hospital Episode Statistics, Ref = Reference, ODS = Operational Data Store, PbR = Payment by Results, SEM =SUS Extract Mart

Figure 3.1: The Hospital Episode Statistics (HES) data processing cycle[1]. Modified from The HES Processing Cycle and Data Quality (2).

‘Pseudonymisation’ refers to the way in which NHS Digital deterministically links new individual inpatient records to existing records in the HES database and belong to the same person, which they do on a monthly basis. NHS Digital use a matching algorithm of the NHS number, date of birth, sex, postcode, hospital provider code, and local patient ID (‘identifiers’) (149). This algorithm involves three ‘passes’, that is, if two records do not match on all variables, there are two other combinations of variables that can be deemed a match. For each data extract, a unique HES ID variable is created per patient so that data may be analysed longitudinally, and so that the HES ID of an individual in one extract does not match that of the same individual in another extract. Before the extract is sent to the user variables of personal information, such as date of birth or postcode, are removed (149).

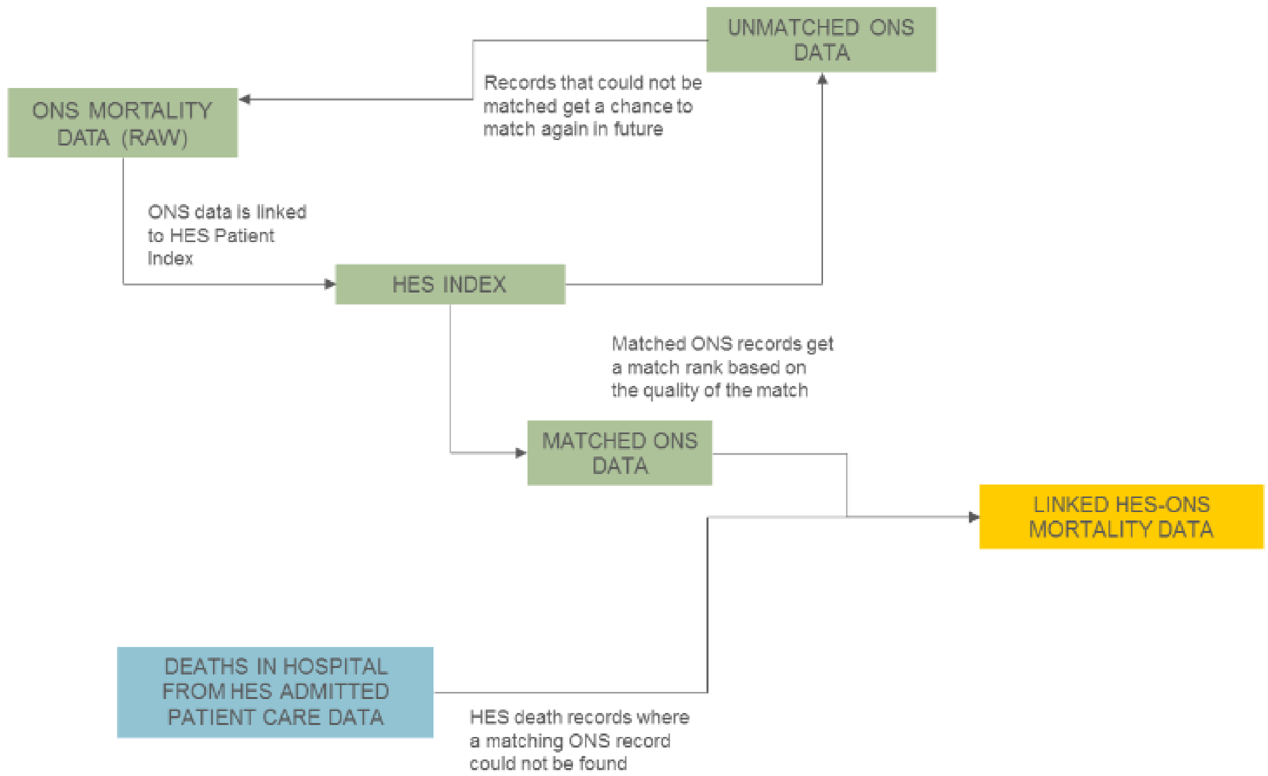
Figure 3.2 shows the process for creating ONS mortality data from death certificates. When a death occurs, a clinician certifies the death by providing a Medical Certificate of Cause of Death, after which the death itself (and cause) are registered by an ‘informant’ (usually a close relative). Deaths in England and Wales are required to be registered within 5 days of their occurrence. Information about registered deaths is then retrieved by the ONS through Register Online. The exception is when the cause of death requires review by a coroner. In this case the coroner may decide the cause is clear and send the case back to the doctor, or request a post-mortem and if the cause is still unknown, an inquest. Difficulties in ascertaining cause of death and delays in registration have implications for interpreting analyses using ONS mortality data (discussed further in Section 3.3.6).



Modified with permission from a presentation slide of Claudia Wells, recent Head of Mortality Analysis at Office for National Statistics (personal communication)
*It is possible for the coroner to adjourn the inquest and carry out an 'accelerated registration' of death, whilst awaiting outcome of any criminal proceedings (150).

Figure 3.2: The ONS mortality data processing cycle

The ONS update their mortality data on a monthly basis, and send them to NHS Digital, who link these data to their latest version of HES (Figure 3.3). NHS Digital use a similar algorithm as for linking episodes for the same individual within HES, based on date of birth, sex, NHS number, and postcode (148). Most information on deaths in linked HES-ONS data (those used in Studies I, II, and III of this thesis) come from ONS mortality data: 2% of deaths are not present in the ONS mortality data and are identified through HES (148).



From "A Guide to Linked Mortality Data from HES and the ONS", Health and Social Care Information Centre 2015

Figure 3.3: Process to match HES inpatient data to ONS mortality data[2].

3.3.3 Episodes, admissions and diagnoses in HES data

The minimal unit in HES is a 'Finished Consultant Episode'. This is a patient case that has been dealt with by an individual consultant (referred to in this thesis simply as an 'episode'). An 'admission', sometimes referred to as a 'spell' in NHS Digital literature and other research (151), is defined as an uninterrupted inpatient stay at a hospital site and may include one or more episodes if the patient was seen by multiple consultants during the same hospital stay. Diagnostic codes in HES are derived from diagnoses given by the clinician within discharge notes, including comments of causes and mechanisms of injuries.

ICD-10 diagnosis codes

HES ID	Start date	Calendar year	HES year	Original admission number	New admission number	Old episode number	New episode number	Sex	Age	Diagnosis 1	Diagnosis	Diagnosis 3	…
1	18/06/1997	1997	1997	1	1	1	1	M	10	S5240	W199	.	…
1	18/03/2000	1999	2000	2	2	1	1	M	11	S009	W139	.	.
1	19/03/2000	1999	2000	3	2	1	2	M	11	S009	.	.	…
2	10/08/2009	2009	2009	1	1	1	1	F	15	Z138	F819	F919	…
2	11/08/2009	2009	2009	2	1	1	2	F	15	F819	.	.	…
2	12/08/2009	2009	2009	3	1	1	3	F	15	F819	.	.	…
2	13/09/2009	2009	2009	4	2	1	1	F	15	F819	.	.	…
2	15/09/2009	2009	2009	5	3	1	1	F	15	F819	.	.	…
2	09/02/2010	2010	2009	6	4	1	1	F	15	F819	.	.	…

Figure 3.4: Example of HES data structure and diagnoses

Diagnoses are recorded in HES using ICD codes from the tenth version (ICD-10; since 1995) (152), comprising of one letter and up to three digits to indicate the specific disease, and grouped in 'chapters'. For example, T74.0 represents 'Neglect or abandonment' and comes under Chapter XIV of the ICD-10: 'Injury, poisoning and certain other consequences of external causes'. Figure 3.4 provides a snapshot of how HES episodes (rows), admissions and diagnoses would appear for two hypothetical adolescents. Since April 2007, each episode in HES can have up to 20 ICD-10 codes entered to give a detailed account of the episode (Figure 3.4; seven codes in April 1997-March 2002, 14 in April 2002-March 2007) (153). In most cases (~90% of episodes), four or fewer ICD-10 codes are entered (154). The HES data dictionary defines the primary diagnosis of an episode as the first ICD-10 code entered (155).

3.3.4 Causes of death

Causes of death in ONS mortality data are captured through information from the death certificate. Figure 3.5 provides an example of the fields of a death certificate. The primary cause of death is recorded under the field 1(a) 'Disease or condition directly leading to death' (Underlying cause in the ONS mortality dataset). Other causes which are related to the primary cause (fields 1(b) and 1(c)), are recorded in the order that they led to each other (Cause 1, Cause 2,… in the ONS mortality dataset). Conditions which did not lead directly to death but could have been related are also recorded in the certificate (field 2), and recorded in the ONS mortality dataset under Cause variables (i.e., direct and indirect causes are indistinguishable in the dataset). All causes were recorded in the ONS mortality dataset (thus in HES-ONS) in ICD-9 coding format in 1979-1999, and have been recorded as ICD-10 since 2001 (both ICD-9 and ICD-10 were used in 2000) (156).

HES ID	Start date	New admission number	New episode number	Sex	Age	Date of death	Underlying cause	Cause 1	Cause 2	Cause 3	...
1	18/06/1997	1	1	M	10	.	.	.	.	.	...
1	18/03/2000	2	1	M	11	.	.	.	.	.	.
1	19/03/2000	2	2	M	11	.	.	.	.	.	...
2	10/08/2009	1	1	F	15	01/02/2012	V090	J80	K918	Y832	...
2	11/08/2009	1	2	F	15	01/02/2012	V090	J80	K918	Y832	...
2	12/08/2009	1	3	F	15	01/02/2012	V090	J80	K918	Y832	...
2	13/09/2009	2	1	F	15	01/02/2012	V090	J80	K918	Y832	...
2	15/09/2009	3	1	F	15	01/02/2012	V090	J80	K918	Y832	...
2	09/02/2010	4	1	F	15	01/02/2012	V090	J80	K918	Y832	...

Specimen certificate (top) with permission and courtesy of Claudia Wells, recent Head of Mortality Analysis at Office for National Statistics (personal communication)

Figure 3.5: Specimen death certificate for England and Wales and example of how certificate data may be recorded in HES-ONS

3.3.5 Data extract for this thesis

I obtained a HES-ONS data extract from the NHS Digital for the financial years 1997-2011 (i.e., April 1st 1997 to March 31st 2011). The data included all admissions for patients aged up to 30 years old (inclusive), and therefore allowed me to study admissions for individuals throughout their adolescence (10-19 years old), and for at least a decade into adulthood. For example, an adolescent who was 19 years old in April 1997 could be observed until they were 30 years old in April 2008. As the data were pseudonymised, I did not require research ethics approval or patient consent according to the Medical Research Council's and NHS Research Authority's decision tool (157). Though HES inpatient data have been collected since 1989, I requested access to an extract dating from 1997, as HES data were not available with admissions linked to the same person before this year. The data cleaning procedure that I employed for this extract is provided in Appendix C.1.

Population cohorts

For each of the three studies in this thesis (I, II and III), I defined a cohort who had at least one emergency admission for adversity-related or accident-related injury during their adolescence. I first identified all adolescents with emergency admissions for injury. I defined an adolescent as a 10-19 year old, the definition used by the WHO (158). Age (on the day of admission) was available for all episodes in HES-ONS data. I describe how I identified emergency admissions and (all types of) injury later in this section. I then applied different criteria, to create two separate study cohorts (the first for Study I, the second for Studies II and III) so that for each study, I could answer the corresponding research question whilst also maximizing the amount of HES-ONS data used.

Cohorts for Study I to III are described in further detail in Chapters 4, 6 and 7, respectively.

Unit of analysis: the admission

All analyses for this thesis were based on admissions rather than episodes, because information on diagnoses may have been duplicated across episodes belonging to the same admission. For example, in Figure 3.4 the first adolescent (HES ID = 1) had two episodes, and both diagnoses were recorded as ICD-10 code S009 ('Superficial injury of the head, part unspecified'). These two records belonged to the same admission and therefore were likely to relate to the same head injury. NHS Digital acknowledges that analysing multiple episodes on regular attendees can 'artificially inflate the figures for certain diagnosis or procedures' (and therefore reports admissions activity alongside episode counts) (151, 159). Therefore, I treated admissions as the unit of analysis but retained all (non-duplicated) information available from constituent episodes of each admission, so that no information was lost.

In the same way that multiple episodes from the same admission may be related to the same medical problem, so may multiple admissions from the same adolescent when they are chronologically close together. For example, if a patient was transferred from one hospital site to another, two admissions were recorded for that patient, rather than two episodes within one admission. Further, day cases and their emergency re-admissions could occur on the same or the following day. In these situations, information may have been duplicated (160). For example, in Figure 3.4 the second adolescent (HES ID = 2) had six admission records containing the ICD-10 code F32 ('Moderate depressive episode'). However, five of these six records occurred within the same week and were likely to be related to the same depressive episode.

To avoid over-estimating the number of admissions, I re-defined a single admission to be a hospital stay where the patient could stay at multiple hospitals due to transfer, and where during a stay they could be discharged and re-admitted within one day. For multiple admission records relating to the same hospital transfer (identified by the variable ‘method of admission’), or admissions within one day of each other (i.e., any admissions that did not start at least two days after the previous admission, identified by start and discharge dates of admissions), I combined their records. Combining of admissions is common practice in research involving HES (151, 161, 162). Figure 3.6 shows total numbers of episodes, original admissions, collapsed admissions, and adolescents in the HES-ONS extract, for those who had an emergency admission for injury. This figure illustrates that by treating collapsed admissions (n=4,169,736) rather than episodes (n=4,673,135) as the unit of analysis, the calculated number of hospital encounters was reduced by ~500,000.

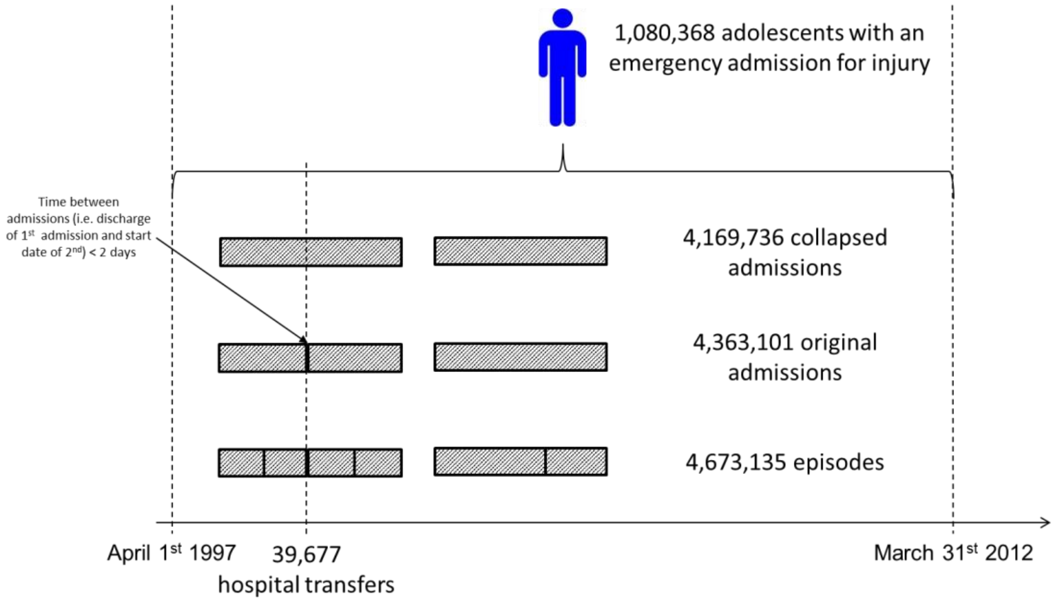


Figure 3.6: Structure of episodes and admissions within HES-ONS (April 1997-March 2012)

Defining an emergency admission for injury

An admission was defined as being an 'emergency' (acute/unplanned) admission if its first episode had a record indicating that the adolescent was admitted via A&E, the GP, a bed bureau[3], and categories other than an elective route, hospital transfer or special waiting list (155).

An admission was defined as being for injury if the first episode's record contained an 'S' or 'T' ICD-10 code. Both S and T codes come from Chapter XIX of the ICD-10 ('injury to a specific body part'). A 1993 WHO report suggest that injury should be defined using both Chapter XIX and XX codes of the ICD-10 (163, 164). However, the current WHO ICD-10 web application states that Chapter XX is merely an adjunct to Chapter XIX and other codes (165). Therefore, the presence of an ICD-10 Chapter XX code alone (without also a Chapter XIX code), did not necessarily indicate an injury.

[3] Bed bureaus are points of contact for a GP to refer patients for urgent admission to hospital.

Capturing adversity-related injury (exposure)

I defined an admission for adversity-related injury as an admission for injury where the record contained ICD-10 codes for violence, self-harm, or drug/alcohol misuse. These three types of adversity were each defined by clusters of codes provided in Appendix C.2.

Because different combinations of types of adversity-related injury are of interest in this thesis (Study I) (e.g., the proportion who were admitted with both self-inflicted and drug/alcohol-related injury), I created coding clusters such that they were mutually exclusive. When a code could be included in two or more coding clusters (e.g., Y15 ['poisoning by and exposure to alcohol'] in either the self-inflicted injury or drug/alcohol misuse clusters), I included the code in one cluster only, based on the likely primary mechanism/intent of the adolescent on a case-by-case basis. For example, Y15 formed part of the sub-chapter 'self-harm with undetermined intent'. It is possible that the adolescent misused alcohol and accidentally suffered alcohol poisoning. Alcohol misuse was definite, but deliberate self-harm was not. Therefore, I included Y15 in the drug/alcohol misuse cluster. Mutually exclusive clusters ensured that an adolescent could only be considered to have been admitted with multiple types of adversity-related injury if they had at least two separate recordings of adversity-related injury at their admission(s).

I created a cluster of codes for 'violence', by modifying a published cluster of codes that had been used to estimate the incidence of admissions for 'victimisation' in 0-18 year olds, and had been validated against medical notes (154, 161, 166-168). This previously-developed cluster for victimisation included codes for direct violence, other forms of maltreatment (e.g., 'Effects of other deprivation [e.g. extreme neglect]'), undetermined causes of injury (e.g., 'Events of undetermined intent'), and adverse social circumstances that would trigger consideration of maltreatment by caregivers (e.g., 'Neonatal withdrawal symptoms from maternal use of drugs of addiction'). Victimisation was most likely to be present as maltreatment in young children and as peer-to-peer assault in adolescents (168). Therefore, in this thesis the cluster of codes for violence contained the same codes as the original cluster for victimisation, except that I removed codes for adverse social circumstances (which in adolescents, was unlikely to necessarily indicate violence, even if coupled with injury).

I defined self-harm using a cluster of codes that mentioned either 'self-harm' or 'self-poisoning'. This cluster contained the same codes as for a study by Wilkinson *et al* (described in Section 1.4.1) (52). In addition, I included the code Z91.5 ('previous history of self-harm'). Though past self-harm may not have triggered an admission, its recording indicated some clinical concern. As self-harm is extremely rare under the age of 10 (8), I assumed that any 'extra' self-harm that Z91.5 captured at admissions between 10 and 19 years old, beyond other codes in the self-harm cluster (those of Wilkinson *et al*) took place during adolescence. As a sensitivity analysis, I estimated the prevalence of self-inflicted injury during adolescence using the cluster both with and without Z91.5 (Chapter 4). By excluding the code Z91.5, the prevalence of self-inflicted injury decreased by 1.0%.

Drug/alcohol misuse was defined by a cluster of codes that mentioned 'drugs', 'alcohol', 'noxious substance', or 'solvent'. I found no studies that had previously validated a cluster of ICD-10 codes for capturing drug/alcohol misuse against other clinician records in adolescents. For this thesis, I defined a cluster which included codes that mentioned *any* drug or alcohol use, which coupled with an emergency admission to hospital for injury would indicate that the injury was drug/alcohol-related. This cluster included all of the 20 codes of Chowdry *et al*'s study of admissions to hospital in England for drug/alcohol misuse in 12-19 year olds (Table 1.2; except for those related to self-inflicted injury) and over 100 extra codes.

I used all diagnosis codes (up to 20) at all episodes within an admission to capture *any* indication of exposure to adversity or of adversity-related behavior. For example, if an adolescent was admitted for injuries from a vehicle accident (recorded as a primary diagnosis) and suspected self-harm was recorded in elsewhere in the admission record, the self-inflicted injury would still be captured.

Capturing accident-related injury (comparison group)

In all three studies, I compared outcomes for adolescents admitted with adversity-related injury to those for adolescents admitted with accident-related injury. An admission for accident-related injury was identified using a cluster of codes for accidents (Appendix C.2), excluding any codes from the adversity clusters. The cluster of codes for accidents contained all codes from the ICD-10 *Accidents* subchapter (i.e., a distinct chapter) (146, 163).

Capturing death and emergency re-admissions (outcomes) in HES-ONS

The outcome in Study I was an emergency admission for adversity-related injury during adolescence. The outcomes for Study II were deaths and emergency re-admissions at least one day after discharge from the emergency admission for adversity-related (or accident-related) injury in question. For Study III the outcome was cause-specific death.

A variable in HES-ONS indicated if an individual had a death record, and another indicated the date of death (if applicable). For each individual, emergency re-admissions (additional data rows in HES-ONS) after the emergency admission for adversity-related (or accident-related) injury in question could be identified through the pseudonymised HESID.

As described in Section 3.3.4, the underlying and up to 15 other contributing causes of death were recorded in HES-ONS data in ICD-9 and ICD-10 format, using information from death registrations. In Study III, I classified deaths into the following categories:

- adversity-related (homicide, suicide, drug/alcohol-related)
- accidental (not adversity-related)
- ‘other deaths’ (not considered to be adversity-related or accidental)

Adversity-related deaths and sub-types (e.g., homicide), and accidental deaths were defined using clusters of ICD codes (Appendix C.3). These clusters differed to those for injury at the index admission in two ways. First, clusters for cause of death categories included ICD-9 codes. Second, the cluster for suicide included ICD codes for events of undetermined intent (ICD-9 codes E980 - E989 and ICD-10 codes Y1-Y34; which the cluster for self-inflicted injury at the index admission did not). These codes were included for the suicide cluster because a coroner could only declare death to be a suicide if there was written (or similar) proof of suicidal intent (150). Therefore, many deaths of undetermined intent may have been in reality, suicides. Using codes of undetermined intent is well-established within suicide research (90), and recommended by the ONS (169).

Covariates: demographic factors and chronic conditions

The prevalence of adversity in the general population has been reported to substantially differ by age, sex and deprivation (socio-economic status) (6, 8, 9, 51), and has been shown to be at least moderately associated with ethnicity and chronic condition status (170-172). In all three studies, I included age, sex, ethnicity, deprivation and chronic (health) condition status. Age at the time of admission, sex, ethnicity and area-based deprivation were available as individual variables in the HES-ONS extract. I captured chronic condition status from HES admission records, using a cluster of ICD-10 codes (described later in this section).

For all three studies, age at the index admission for injury was classed in meaningful groups for analyses. In Studies I and II, age was grouped as 10-14, 15-17 and 18-19y, to represent different stages of development: onset of puberty (10–14 years) (173), ages of secondary school examinations (15–17 years) (174, 175), and the legal age for buying alcohol (18–19 years) (176). For Study III, age was grouped as: 10-15, 16-17 and 18-19y, to take into account admission thresholds for self-harm, since national guidelines mandate admission for under 16 year olds (57).

Ethnicity was usually classed by the patient (the HES data dictionary indicates that this was a patient-reported variable).I If the patient declined to answer or were unconscious, the field was completed as ‘unstated’ or ‘unknown’ (155). Ethnicity could be recorded differently between multiple records on the same person. When assessing an individual’s ethnicity based on different admission records, I prioritised ethnicity recorded during adolescence (i.e., between 10 and 19 years old), rather than at other ages where admission records were also available (0-9 and 20-30 years old), as these values were more likely to represent self-perceived ethnicity at the time of the index admission for injury.

Ethnicity was provided in HES-ONS as 10 categories until 2001 and 16 categories after 2003 (Table 3.1); 2001-2003 was classed as a transition period between the two systems (177). For all three studies, I classified adolescents into six broader categories: White, Black, Asian, Mixed, Other or Missing. Thus ethnicity was consistently categorised for the entire dataset. If there was evidence of an association between one of these broad ethnic categories (e.g., Black, with a higher/lower incidence of adversity-related injury or risk of future harm), I examined the associations of sub-categories of ethnicity (e.g., Black Caribbean).

Table 3.1: Ethnic categories used in HES and ONS, by time periods and mapped on to categories used in this thesis

HES: from 1995-96 to 2000-01	ONS: 1997-2012 HES: From 2001-02 onwards	Ethnicity categories used in this thesis
White	British (White) Irish (White) Any other White background	White
Black – Caribbean Black – African Black – Other	Caribbean (Black or Black British) African (Black or Black British) Any other Black background	Black
Indian Pakistani Bangladeshi Chinese	Indian (Asian or Asian British) Pakistani (Asian or Asian British) Bangladeshi (Asian or Asian British) Any other Asian background Chinese (other ethnic group)	Asian
Not applicable	White and Black Caribbean (Mixed) White and Black African (Mixed) White and Asian (Mixed) Any other Mixed background	Mixed
Any other ethnic group	Any other ethnic group	Other
Not given Not known	Not stated Not known	Missing

Deprivation was provided in HES-ONS data via Index of Multiple Deprivation (IMD) scores that were derived from admission records (178). The IMD score was a ranking of deprivation within the area, based on the patient's residence postcode, which came under a particular Lower Super Output Area (LSOA). A higher score indicated a higher estimated level of deprivation (179). I classified IMD scores from the HES-ONS dataset into quintiles, using cut-offs for the total population (of any age) in England that were provided in the HES data dictionary (155).

There were no IMD quintile cut-offs for England available for adolescents, specifically. Each quintile cut-off was unlikely to map directly on to what the cut-offs would be for adolescents, which caused difficulty in interpretation of results related to deprivation. For example, in Study I the cohort included more adolescents from the most deprived quintiles, compared to less deprived (see Table 4.3 and Table 4.4). This result may indicate that more deprived adolescents were more likely to be admitted to hospital with adversity-related or accident-related injury than less deprived adolescents, but could also be partly a result of mis-calibration of deprivation quintile cut-offs (from patients of all ages to the sub-population of adolescents).

Chronic conditions were defined using a cluster of ICD-10 codes which were previously developed for the Royal College of Pediatrics and Child Health (RCPCH) report on Child Deaths in the UK. The report was of a cohort study exclusively in children who died (180). The cluster was developed in consultation with a panel of clinicians, with the aim that the cluster included any conditions typically requiring medical treatment for at least one year. For this thesis, I modified the cluster to exclude any codes that were already in the clusters for violence, self-harm or drug/alcohol misuse (this modified cluster is described in Appendix C.4). The original cluster in the RCPCH report included codes that indicated a chronic condition only if they appeared at an admission with a length of stay greater than 3 days that was within 30 days before the date of death (180). I excluded these codes from the cluster for chronic conditions in this thesis, because unlike the cohort in the RCPCH report, some adolescents did not die. Therefore, the estimated prevalence of chronic conditions for adolescents in this thesis was lower than that estimated in studies of comparable populations (181).

No values for age were missing in the HES-ONS extract, and it was not possible for chronic condition status to be missing because of how it was derived (a lack of chronic condition codes within the patient's record could indicate either unrecorded status [missing] or no chronic condition at all). For missing values of sex, ethnicity and deprivation, I replaced these values with the modal value at 10-19 years old, where possible (and at 0-30 years old if this value was still missing). For some adolescents, sex, ethnicity or deprivation was missing for all of their records, and so these values could not be replaced.

3.3.6 Strengths and limitations of HES-ONS for this thesis

The HES-ONS dataset had several strengths for addressing the aims of this thesis. Most individuals who were admitted to a hospital in England would have been admitted to a NHS hospital: 98-99% of hospital activity in England is funded by the NHS (182). Therefore, HES-ONS data captured the majority of the population of interest (all adolescents who had an emergency admission to hospital in England for injury). The large numbers of adolescents in HES data (approximately one million admitted with injury) allowed the investigation of different types of adversity-related injury, by age, sex, and other demographic factors such as ethnicity. HES-ONS data also captured the majority of deaths before 31 years old (the age limit of the data extract) in the population of interest (one of the main outcomes for this thesis). Therefore, the estimation of risks of death was not hindered by small numbers of events (183).

Another strength was that HES data were longitudinally linked records, which allowed identification of all admissions on each adolescent during the periods of each study. Previously, studies have reported the *incidence* of admissions (rather than prevalence) for separate types of adversity-related injury in young people (51, 52), but some of these admissions could be from the same adolescents. In this thesis, the calculations of prevalence estimates were based on adolescents (not admissions) even if they had multiple admissions. In addition, linked records allowed identification of the outcome of re-admissions.

Third, linked HES-ONS data covered a recent time-period of fifteen years (from 1997 to 2012). Analysing a recent extract of HES-ONS allowed estimation of the prevalence of an admission for adversity-related injury that would be relevant to today's adolescent population. The long time coverage of HES-ONS allowed estimation of ten-year risks of death and re-admission. Previously, risks of re-admission and all-cause death have only been reported up to 18 months (184, 185).

Fourth, HES-ONS data were routinely collected administrative data (i.e., not collected for research purposes). Clinicians, hospital-based coders, coroners, NHS Digital, and ONS had little association with the research that occurred at the end of the processing cycle. Therefore, the possibility of researcher bias was reduced when compared with analysing prospectively collected data (i.e., the majority of studies summarised in Section 1.5). Information about admissions and deaths was prospectively recorded in HES, and near to the time of death in ONS. Therefore, recall bias was unlikely when compared with previous surveys of adolescents regarding previous risk-taking behaviours and healthcare contacts (91, 183).

Finally, HES-ONS data have become well established in research over the past two decades, and have therefore been analysed with an understanding of the strengths and limitations of the dataset. Data dictionaries made available by NHS Digital have provided information on how data are recorded (e.g., how the ethnicity variable may be interpreted) (155). Reports have been published about the levels of accuracy of HES data (186-188), and of causes of death in ONS mortality data (189). ICD codes that were used to record diagnoses in HES, have been previously used in research to identify violence, self-harm and drug/alcohol misuse (50-52), which used to inform development of clusters of ICD codes specifically for this thesis.

Although there were numerous strengths to using HES-ONS data for this thesis, there were also limitations. First, ICD-10 codes were shown in studies worldwide to be only moderately sensitive for identifying adversity (166, 190-197). Studies validating child maltreatment findings in health databases found maltreatment to be consistently under-reported (194, 195), either by being recorded in case-notes but not coded, coded wrongly, or not being recorded at all (191, 196). Therefore, coding clusters in HES-ONS were unlikely to be very sensitive and were more likely to capture adolescents with the most severe forms of adversity (i.e., low sensitivity but high specificity). Therefore, it was likely that some adolescents admitted with adversity-related injury were classed as having been admitted with accident-related injury instead. This misclassification would lead to under-estimates of the prevalence of adversity-related injury, as well as under-estimates of relative risks of outcomes between adversity-related and accident-related injury.

Although ICD-10 codes provided some level of consistency in diagnoses, they did not account for variation between individual clinicians in how they recognised and responded to presentations for adversity-related injury (198-201). This response and thus ‘crossover’ between the adversity-related and accident-related injury groups may have differed for different adolescent sub-groups (199, 202). For example, in a cohort study of 13-19 years olds treated in a US ED, clinicians were more likely to test for alcohol involvement if the patient was male or older (199). If this was the case for hospital clinicians in England, the prevalence of our relative risks of outcomes following adversity-related injury would have been under-estimated in male or older adolescents. Therefore, estimates in these groups (e.g., older males) should be interpreted bearing such biases in mind.

Second, during both linkage within the HES database and linkage of HES to ONS mortality data, errors may have been introduced into the datasets through ‘false’ or ‘missed’ linkage. False-matches occur when two records are joined together when they do not truly belong to the same individual. This was possible in HES when two individuals were given the same NHS number or local patient ID, when data were entered incorrectly for one of the candidate records, or through coincidence (i.e., two individuals had the same date of birth, sex, postcode and hospital provider code).

Missed matches occurred when two records that belonged to the same individual were not identified as such via the matching algorithm, and thus remained unlinked. This was possible when identifier data were recorded in different formats, when data on identifiers were missing, or when data for one of the candidate records were entered incorrectly. False matches could lead to over-counting of numbers of admissions or over-estimation of risks of death or re-admission. Missed matches could lead to under-counting or under-estimation.

Hagger-Johnson *et al* used the same algorithm that was used to link episodes in HES data to link episodes within another national administrative database that was identifiable (the Paediatric Intensive Care Audit Network), and estimated 0.1% false match and 3.8% missed match rates (203). The authors also estimated that male adolescents and those of Missing or Mixed ethnicity were 1.4 to 2.6 more likely to incur false matches[4], and that missed matches were more prevalent among adolescents of certain ethnic minorities or from areas of relatively high deprivation (203). Based on this study, I assume that levels of missed matching were greater than false matching in the HES-ONS extract. Therefore, I assume that the estimated prevalence of adversity-related injury, and risks of subsequent harm, were under-estimated in this thesis, especially for those of ethnic minority or residents of areas of relatively high deprivation.

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[4] The authors identified a false match in this group when two candidate admissions were simultaneous.

Third, as HES-ONS data were administrative and not collected for research purposes, there are limited covariates available (described in Section 3.3.5). There are potentially several other factors (e.g., registration with a GP), that may have confounded the estimated association between adversity-related injury and outcome.

Fourth, levels of recording of HES data have improved over time (145, 160, 204). The PbR initiative and 4-hour maximum wait policy introduced in 2003 were likely to have encouraged increased recording of diagnoses and admissions. This initiative may in turn have led to increased recording of the true incidence of adversity-related injury. Therefore, estimates of the prevalence of adversity-related injury and risks of re-admissions were likely to be closer to the 'true' prevalence and risks when estimated from data in later years. To investigate estimates of prevalence in Study I altered over time, I estimated the prevalence for the earliest and latest possible time periods, i.e., adolescents who were 10 years old in 1998 compared with those who were 10 years old in 2002. The population prevalence of adversity-related injury at 10-19 years old differed by one decimal point (see Section 4.4.1).

Finally, HES-ONS was less likely to capture deaths of unusual circumstances (e.g., homicide) than other types of death, due to a need for further investigation which could have delayed registration by a year or more in some cases (205). An ONS report of time delays for death registrations showed that for deaths where the cause was 'external', 13% were registered within the cut-off of five days, with a median delay of 139 days (206). If adolescents admitted with adversity-related injury were more likely to die from causes that required investigation than accident-related injury (189), risks of death between adversity-related and accident-related injury would have been under-estimated.

3.4 Office for National Statistics (ONS) population mid-year estimates

3.4.1 Background

In Study I, I estimated the prevalence of emergency admission for different types of adversity-related injury, during adolescence. This analysis required population denominators, which I derived from ONS population mid-year estimates for England (which approximate annual total numbers of the UK population on 30th June per year) (207).

These estimates were derived by the ONS from census data that was collected every ten years since 1801 (except in 1941 where this census was interrupted by war) (208). These data were collected for informing local authorities and the government to assess current service need and make projections for the future.

3.4.2 Data processing

The ONS uses decennial census counts to estimate counts per year. Between these ten-year counts, the ONS estimates mid-year counts by adjusting for birth and death counts obtained from birth and death registrations, and emigration and immigration data obtained from other sources such as the International Passenger Survey and visa applications. These mid-year counts are updated on a monthly basis.

3.4.3 Data extract for this thesis

ONS mid-year population estimates were available freely online as Excel tables (209). I used mid-year estimates for the years 1998-2002. Figure 3.7

illustrates how ONS mid-year population estimates appeared online, by age and sex.

	A	B	C	D	E	F	G	H	I	J	K	L	M
1		1998			1999			2000			2001		
2	Age	Persons	Males	Females	Persons	Males	Females	Persons	Males	Females	Persons	Males	Females
3	**10-14**	**3,125,402**	**1,600,402**	**1,525,000**	**3,173,879**	**1,624,145**	**1,549,734**	**3,197,772**	**1,636,456**	**1,561,316**	**3,238,061**	**1,658,330**	**1,579,731**
4	10	648,055	331,692	316,363	642,561	328,318	314,243	649,563	332,563	317,000	660,955	338,658	322,297
5	11	631,246	322,545	308,701	649,687	332,541	317,146	642,511	328,580	313,931	650,382	333,212	317,170
6	12	621,482	318,010	303,472	632,635	323,164	309,471	649,415	332,681	316,734	642,727	329,004	313,723
7	13	624,705	320,814	303,891	622,987	318,546	304,441	633,373	323,756	309,617	650,171	333,173	316,998
8	14	599,914	307,341	292,573	626,009	321,576	304,433	622,910	318,876	304,034	633,826	324,283	309,543
9													
10	**15-19**	**2,984,211**	**1,512,677**	**1,471,534**	**2,996,729**	**1,521,680**	**1,475,049**	**3,002,327**	**1,531,445**	**1,470,882**	**3,045,000**	**1,558,466**	**1,486,534**
11	15	595,692	304,375	291,317	601,147	308,109	293,038	624,520	321,132	303,388	625,706	320,819	304,887
12	16	596,787	305,123	291,664	596,805	305,110	291,695	601,375	308,645	292,730	629,729	324,331	305,398
13	17	607,660	309,735	297,925	598,718	306,428	292,290	595,597	304,876	290,721	607,690	312,556	295,134
14	18	604,016	305,685	298,331	600,797	304,318	296,479	586,166	299,152	287,014	593,746	303,707	290,039
15	19	580,056	287,759	292,297	599,262	297,715	301,547	594,669	297,640	297,029	588,129	297,053	291,076

Figure 3.7: Example of ONS mid-year population estimates by sex and age

Deriving population denominators

To derive denominators for adolescent girls in the cohort of Study I (Figure 4.1), I calculated the sum of mid-year population estimates for 10 year old females in 1998, 1999, 2000, 2001 and 2002. I repeated this process to provide a denominator for boys.

3.4.4 Strengths and limitations of ONS mid-year estimates for this thesis

At the time of Study I ONS estimates were the only source of data for counts of the entire population in England. The principal strength of these data for Study I was their coverage of the same period of time as the cohort, provided by age and sex.

The ONS also managed national birth, death and migration data on which to based estimates of population counts. Therefore, it was likely that mid-year estimates used in this thesis were reasonably accurate. However, overall estimates of the population of 10 year olds in 1998-2002 were not equivalent to exact population counts. The 1998 and 1999 mid-year estimates were estimated using the 1991 and 2001 census population counts, and birth, death, and migration rates for 1991-2001 (207, 210). Nevertheless, population counts for 10 year old girls and boys did not differ by more than 31,142 between the 1991 and 2001 censuses[5]. The 'true' denominators for 1998-2002 were not expected to differ by more than approximately this number, compared with the derived denominator. When the derived denominators for 1998-2002 were altered by 30,000 less (or more) the estimated prevalence of adversity-related injury did not change by more than a decimal place (see Section 4.4.1).

One potential limitation of ONS data for Study I is that certain sub-groups of adolescents would not be included in population counts. Illegal immigrants and those who have been admitted to hospital when visiting from another country would not be present in this database and thus total population figures for different age and sex groups in ONS will be underestimates of the present population, unless we assume that a similar proportion of the population migrated and visited out of the country at the same time. Homeless adolescents may also not be present in decennial census counts on which mid-year estimates are derived. One would expect these excluded adolescents to be disproportionately susceptible to psychosocial issues, and therefore potentially include disproportionately high rates of adversity.

Another limitation of ONS mid-year estimates was that they were not readily available by covariates of interest that *were* available in HES-ONS data, other than age or sex (e.g. ethnicity or deprivation). Some mid-year estimates split by ethnicity are available for research (211), but not also by age and sex (i.e., by sub-strata of each calendar year, age year, sex, and ethnicity), and only for the period 2002-2009.

[5] Girls: increased from 294,464 to 322,297. Boys: increased from 307,516 to 338,658

Chapter 4 Study I, Prevalence of emergency admissions for adversity-related injury (Objectives 1 and 2)

4.1 Chapter summary

In this chapter I describe analyses for meeting Objectives 1 and 2 of this thesis. I used HES data for 1997-2012 to identify adolescents who were 10 years old in 1998-2002 and had ever been admitted to hospital as an emergency with injury between 10 and 19 years of age (inclusive; the study cohort). To address Objective 1, I identified adolescents who were admitted with adversity-related injury in particular (the numerator), and estimated population prevalence using ONS mid-year estimates to derive denominator values (see Section 3.4.3). To address Objective 2, I calculated the proportions of adolescents admitted with adversity-related injury, who were admitted with more than one type (clusters of codes to capture violent, self-inflicted, and drug/alcohol-related injury were mutually exclusive). Finally, I determined the number of admissions for adolescents admitted with adversity-related injury (total, and number of adolescents with 1, 2, or 3+), and compared it to those for adolescents in the study cohort who were admitted with accident-related injury.

Nine percent of girls and sixteen percent of boys in the HES-ONS data were admitted to hospital as an emergency with injury (12% of all adolescents). Approximately half of the 8% of girls and one-quarter of the 16% of boys were admitted with adversity-related injury (i.e., 4%, or 1 in 25 for both sexes); nearly all of the remaining girls and boys were admitted with accident-related injury. Among those admitted with adversity-related injury, 73% of girls and 38% of boys were admitted with multiple types of adversity-related injury. The most common combination of types was self-inflicted and drug/alcohol-related injuries, which most often occurred at the same admission. Adolescents who were admitted with adversity-related injury were more likely to be admitted more than once, during adolescence. For example, 17% of girls with adversity-related injury were admitted two or more times as an emergency with injury, compared with 5% of girls with accident-related injury.

From these findings, I conclude that adversity-related injury affects a substantial proportion of adolescents (1 in every 25), and that these adolescents are often exposed to multiple types of adversity. Emergency admissions for adversity-related injury are associated with a higher burden on hospital services through the number of admissions, particularly for adolescents admitted with multiple types of adversity. Improved clinical management of adolescents with adversity-related injury could reduce this burden. Strategies could include increased consideration of co-occurring adversity, not just that forming the primary diagnosis at presentation to hospital.

4.2 Introduction

In Chapter 1, a review of studies of emergency admissions for adversity-related injury to hospitals in England during adolescence (Section 1.4) revealed that there were few estimates of the prevalence of such admissions, and none that considered multiple types of adversity-related injury within the same group of adolescents (Section 1.4). Adolescents admitted to hospital with adversity-related injury may be at greater risks of harm compared to other admitted adolescents. However, we do not know the size of this population or its socio-demographic or clinical characteristics.

This chapter describes analyses of Study I used to address Objectives 1 and 2:

1. *Estimate the prevalence of an emergency admission for adversity-related injury (as a whole and by type of adversity-related injury [violent, self-inflicted, drug/alcohol-related]), during adolescence (between 10 and 19 years of age), by sex and other demographic and clinical factors.*
2. *Among adolescents admitted with adversity-related injury, determine the proportion admitted with multiple types of adversity-related injury, either at the same admission, or across multiple admissions during adolescence.*

I also determined the burden on hospital services through the number of admissions associated with this adolescent group, and compared this to the burden for adolescents admitted with accident-related injury.

The main results from this chapter were published in *BMJ Open* (212). The full article is presented in Appendix D.1.

4.3 Methods

4.3.1 Study cohort and admissions

Using HES inpatient data, I derived a retrospective cohort of adolescents who turned 10 years old between 1998 and 2002 (inclusive), so that all individuals could be observed throughout adolescence until 19 years of age (Figure 4.1). Each individual also had to have had at least one emergency admission for injury between 10 and 19 years old. Admissions and emergency admissions for injury were defined as described in Section 3.3.5.

4.3.2 Adolescent groups

Using ICD-10 codes within records for all emergency admissions for injury between ages 10 and 19, adolescents were classified as belonging to either an 'Adversity' group (any violent, self-inflicted injury, or drug/alcohol-related injury) or an 'Accidents Only' group (no adversity-related injury but any accident-related injury) (Figure 4.2). Clusters of ICD-10 codes for violence, self-harm, drug/alcohol misuse, and accidents are provided in Appendix C.2. The remaining adolescents with no adversity- or accident-related injury at emergency admissions between 10 and 19 years old are referred to as adolescents with 'Other Causes' of injury (Figure 4.2).

I further classified the Adversity group into seven mutually exclusive sub-groups: violent injury only, self-inflicted injury only, drug/alcohol-related injury only, violent and self-inflicted injury, violent and drug/alcohol-related injury, self-inflicted and drug/alcohol-related injury, and violent, self-inflicted and drug/alcohol-related injury (Figure 4.2).

Calendar year	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
	0	1	2	3	4	5	6	7	8	9	10	11	12	13
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
	2	3	4	5	6	7	8	9	10	11	12	13	14	15
	3	4	5	6	7	8	9	10	11	12	13	14	15	16
	4	5	6	7	8	9	10	11	12	13	14	15	16	17
	5	6	7	8	9	10	11	12	13	14	15	16	17	18
	6	7	8	9	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**
	7	8	9	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	20
	8	9	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	20	21
Age	9	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	20	21	22
	10	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	20	21	22	23
	11	12	13	14	15	16	17	18	19	20	21	22	23	24
	12	13	14	15	16	17	18	19	20	21	22	23	24	25
	13	14	15	16	17	18	19	20	21	22	23	24	25	26
	14	15	16	17	18	19	20	21	22	23	24	25	26	27
	15	16	17	18	19	20	21	22	23	24	25	26	27	28
	16	17	18	19	20	21	22	23	24	25	26	27	28	29
	17	18	19	20	21	22	23	24	25	26	27	28	29	30
	18	19	20	21	22	23	24	25	26	27	28	29	30	
	19	20	21	22	23	24	25	26	27	28	29	30		

*Striped area represents at w hat ages adolescents and their admissions w ere studied

Figure 4.1: Cohort of individuals who were 10 years old in 1998-2002 and had at least one emergency admission for injury in 1998-2011*

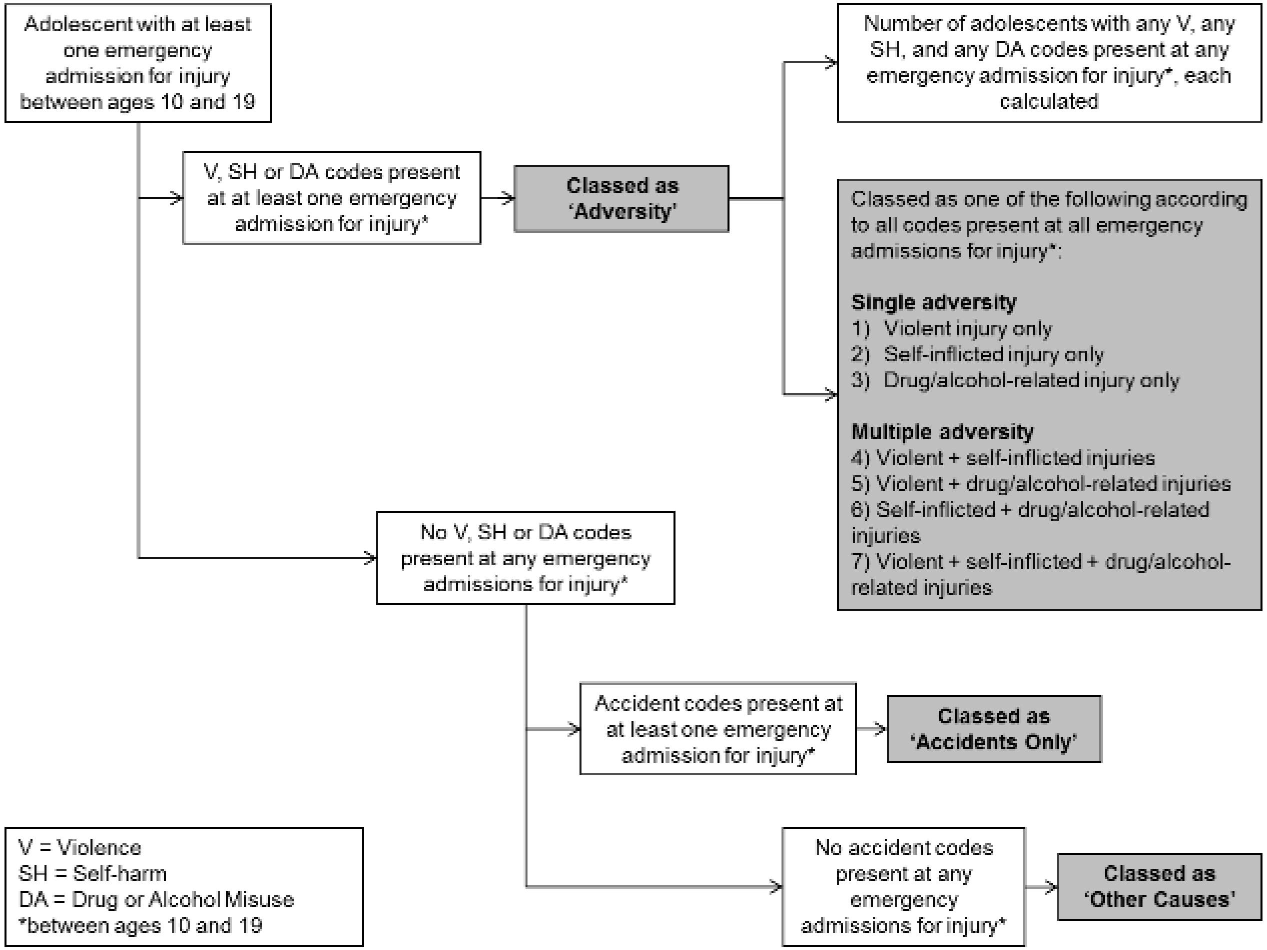


Figure 4.2: Classification of adolescents for Study I: Prevalence of emergency admissions for adversity-related injury (Objectives I and 2)

4.3.3 Adolescent characteristics

I included sex, age (by year and age-groups: 10-14, 15-17, 18-19y), ethnicity (White, Black, Asian, Mixed, Other), deprivation (by quintiles of Index of Multiple Deprivation [IMD] scores), and chronic condition status (yes/no) in analyses. More information about how deprivation quintiles and chronic condition status were derived, reasons for these groupings, and how missing values were handled, are provided in Section 3.3.5.

4.3.4 Population denominators

To estimate population rates of emergency admissions for adversity-related (and accident-related) injury, I derived estimated population counts as described in Section 3.4.3.

I also derived denominator values for age-groups within the cohort. Denominators for 10-14 year olds were the same as for 10-19 year olds (10 year olds in 1998-2002, as 10-14 year olds in the cohort were also all 10 years old during this period). I derived denominator values for 15-17 year olds in a similar way. For example, for 15-17 year old girls, I estimated the population count for 15 year old females in 2003-2007 (Figure 4.1).

4.3.5 Statistical analyses

All analyses were stratified by sex because of well-established differences in the prevalence of violent, self-inflicted and drug/alcohol-related injury, respectively (8, 30, 51, 213).

Objective 1: I estimated the proportion of adolescents in the general population who had an emergency admission for adversity-related injury between 10 and 19 years old. I then calculated the proportions of adolescents from the general population who belonged to the Adversity, Accidents Only and Other Causes groups at 10-19 years of age. I present these proportions by ethnic group, deprivation quintile, and chronic condition status at 10-19 years old.

As there is strong evidence for an association between age and prevalence of adversity in the general population, I repeated the above analyses by age-group and age-year. To report prevalence by age-group, I re-grouped adolescents as Adversity (and subgroups), Accidents Only and Other Causes according to all emergency admissions for injury within age-groups (Figure 4.3). I then grouped adolescents as in Figure 4.3, according to each individual age-year: 10, 11,… 19 years old. I explicitly present population prevalence values by age-groups to provide meaningful estimates, rather than a prevalence value for each year between 10 and 19 years old. I still estimated prevalence by age-year, in order to plot these values over time and describe the general relationship of prevalence with age.

To determine total burden of service use by adolescents who are ever admitted as an emergency with adversity-related injury, I calculated the total numbers of admissions between 10 and 19 years old (and by emergency and non-emergency, and injury and non-injury) for adolescents in the Adversity group. I then compared these numbers to those for the Accidents Only group, which was considered to have 'baseline' rates of admissions. To determine the extent to which individual adolescents may disproportionately contribute to the total number of admissions, I calculated the proportions of adolescents who had none, one, two, or three or more admissions.

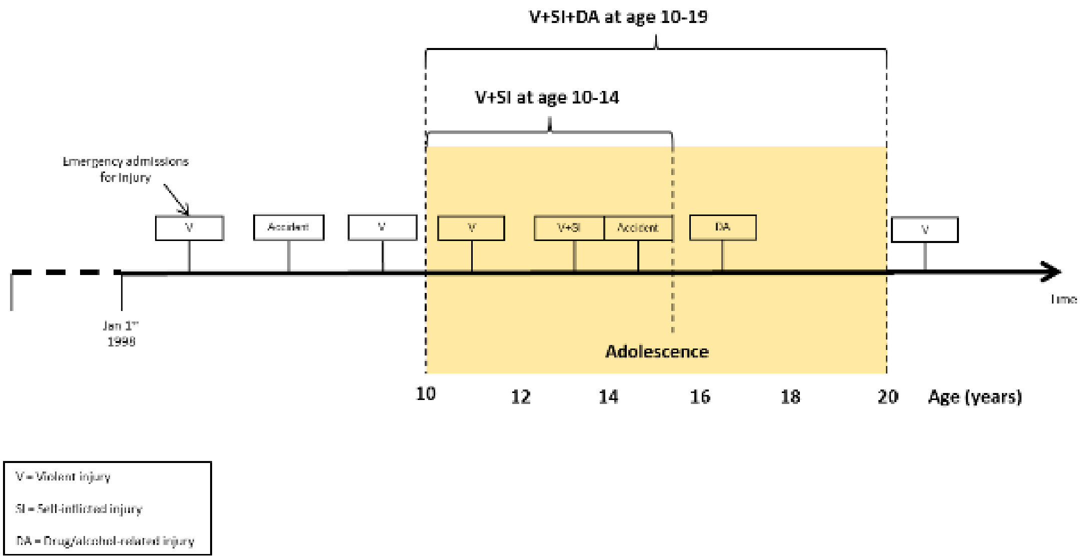


Figure 4.3: Example of classification of an adolescent into adversity-related injury sub-groups according to emergency admissions at different ages

Objective 2: I calculated the proportions of adolescents who were in the Adversity group, by Adversity sub-group (violent injury only, self-inflicted injury only, etc.) (Figure 4.2). I then determined whether adolescents exposed to multiple types of adversity-related injury were likely to have these multiple types seen during the same admission. Within each Adversity sub-group for multiple types of adversity-related injury (e.g., violent and self-inflicted injury), I calculated the number of adolescents who had both types recorded at the same admission (Figure 4.4).

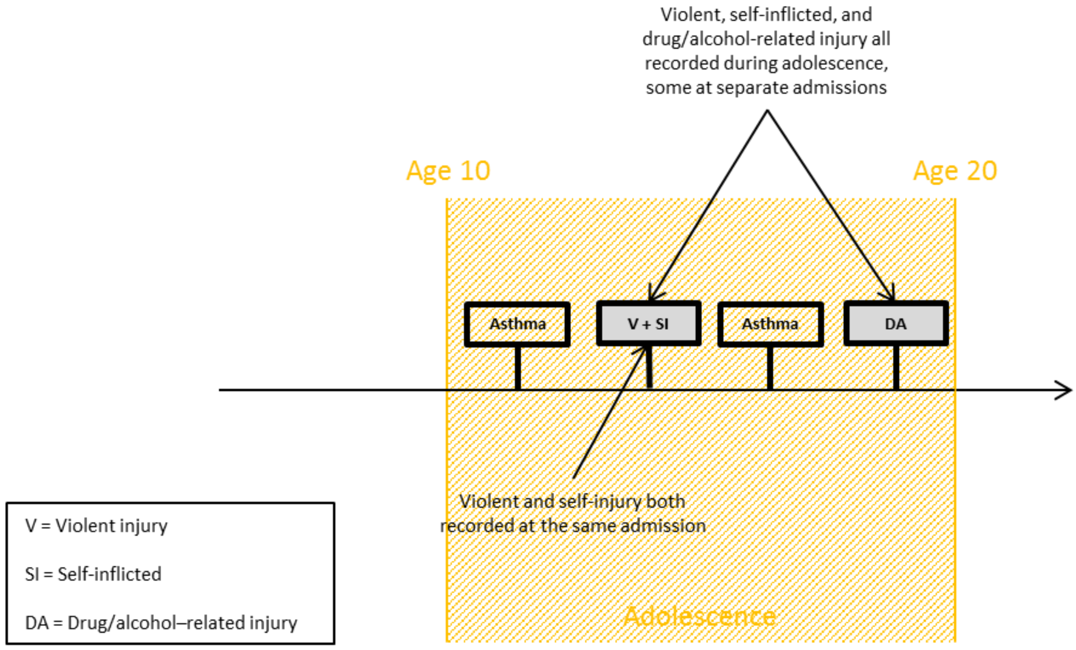


Figure 4.4: Example of how different types of adversity-related injury may occur either at separate or the same admissions during adolescence

I carried out sensitivity analyses, to test the effect of different ways to define adversity-related injury in HES inpatient data (see Chapter 3). I repeated estimations of prevalence of the Adversity, Accidents Only, and Other Causes groups, respectively, as follows:

1) Using only the primary diagnosis code to define injury, adversity and accidents (rather than up to 20 codes in each record)
2) Not including ICD-10 codes Z91.5 ('personal history of self-harm') in the coding cluster for self-inflicted injury.

I calculated 95% confidence intervals (CIs) for all proportions. However, these are not presented in this thesis, since they were all very narrow (within one unit of the sample estimate; e.g., the study cohort represented 12.38% of the general population, and the 95% CI for this was 12.36% to 12.44%). That is, they were too narrow to convey any useful information about uncertainty around estimates.

4.4 Results

There were 402,916 adolescents in the study cohort (802,682 admissions), representing 12.4% (402,916/3,254,046) of the adolescent population. Twice as many boys as girls had an emergency admission for injury during adolescence (144,158/1,588,942 girls in the population [8.7%]; 258,503/1,665,104 boys [16.3%]).

4.4.1 Objective 1: Prevalence of adversity-related injury

One-third of the cohort (140,152, 4.3%, or approximately one in 25 of the population) had a recorded emergency admission for adversity-related injury (the Adversity group), with similar rates between sexes (72,805, 4.6% girls in the population; 68, 403, 4.1% boys) (Table 4.1). The remaining two-thirds of the cohort (261,668, 8.1% of the adolescent population) were adolescents who had emergency admissions for injuries that were not related to adversity. Among adolescents with admissions not related to adversity, 233,907 (89.4%) had accident-related injury (7.2% of the population; the Accidents Only group); 27,761 (10.6%) had no accident-related injury (0.9% of the population; classed as ‘Other Causes’). Adolescents in the Other Causes group were more likely to be affected by a chronic condition between 10 and 19 years old (40%), when compared with the Adversity group (32%) or the Accidents Only group (21%).

Types of adversity-related injury

For adolescents in the Adversity group, the majority of girls were admitted with self-inflicted or drug/alcohol-related injury (self-inflicted: 54,315, 3.3% of the general population; drug/alcohol-related: 66,645, 4.0%, i.e., nearly all of the

4.3% in the Adversity group) (Table 4.1). Boys in the Adversity group were most likely to be admitted with violent or drug/alcohol-related injury (violent: 32,779, 2.2% of the general population; drug/alcohol-related: 41,014, 2.5%).

For both girls and boys admitted with violent injury, the majority were accounted for by assault, rather than maltreatment-related injury or events of undetermined intent (girls: 80.5%, boys: 95.2%; rates of maltreatment-related conditions and events of undetermined intent, which were not mutually exclusive from assault, ranged from 1.1 to 15.9%) (Table 4.1). Most cases of self-inflicted injury were poisonings (girls: 90.5%, boys: 86.7%). For girls admitted with drug/alcohol-related injury, most were had a record of illicit drug use (91.2%). For boys had a record of illicit drug use (64.4%) or alcohol misuse (51.0%).

Table 4.1: Numbers of adolescents* admitted to hospital as an emergency for injury in England (1998-2011), by injury group

Injury group Types of adversity-related injury	Number of adolescents (population prevalence, %)		
	Total	**Girls**	**Boys**
All	402,916 (12.38)	144,158 (8.66)	258,503 (16.27)
Adversity	141,248 (4.34)	72,805 (4.58)	68,403 (4.26)
Any violent injury	39,010 (1.20)	6,211 (0.39)	32,799 (1.98)
Any self-inflicted injury	75,402 (2.32)	54,315 (3.26)	21,087 (1.33)
Any drug/alcohol-related injury	107,659 (3.24)	66,645 (4.19)	41,014 (2.46)
Accidents Only	233,907 (7.19)	59,465 (3.74)	174,267 (11.01)
Other Causes	27,761 (0.85)	11,888 (0.71)	15,833 (1.00)

Due to large denominators, confidence intervals for population prevalence were too narrow to provide any meaningful interpretation and so are not shown.
Injury groups = Adversity, Accidents Only, Other Causes
*Who were 10 years old in 1998-2002.

Table 4.2: Frequency of emergency admissions for sub-types of violent, self-inflicted, and drug/alcohol-related injury in England (1998-2011), among adolescents in the Adversity group

Type of adversity-related injury Sex	Number of adolescents	Number of admissions (% of emergency admissions for injury)			
Violent		Emergency admissions for injury	Maltreatment-related	Assault	Undetermined intent
Girls	6,211	6,267 (100.0)	559 (8.9)	5,662 (90.3)	1,243 (19.8)
Boys	32,799	35,891 (100.0)	380 (1.1)	33,984 (94.7)	2,511 (7.0)
Self-inflicted		Emergency admissions for injury	Poisoning	Non-poisoning	History of self-harm
Girls	54,315	84,414 (100.0)	58,283 (69.0)	5,990 (7.1)	15,083 (23.5)
Boys	21,087	27,786 (100.0)	19,614 (70.6)	3,120 (11.2)	4,696 (16.)
Drug/alcohol-related		Emergency admissions for injury	Environmental drugs	Illicit drugs	Alcohol misuse
Girls	66,645	99,591 (100.0)	983 (1.0)	69,103 (69.3)	19,778 (19.9)
Boys	41,014	48,665 (100.0)	1,062 (2.6)	26,998 (55.5)	21,505 (44.2)

Row percentages do not necessarily add up to 100% as they are not mutually exclusive. For example, an adolescent may have maltreatment-related injury and assault recorded at the same admission.

Likelihood of adversity-related injury by adolescent characteristics

The proportions of adolescents classified to the Adversity group differed by ethnic group, deprivation quintile, and chronic condition status (Table 4.3; Table 4.4).

Girls of mixed ethnicity were more likely to be classed as Adversity (63.2%) than girls belonging to other ethnic groups (e.g., White: 51.8%). The one quarter of girls with missing ethnicity were least likely to be classified into the Adversity group (43.8%) (Table 4.3). Girls living in an area of high deprivation were more likely to be classed as Adversity than girls living in areas of low deprivation (e.g., Most vs. least deprived: 57.3 vs. 42.8%). Those who had a record of a chronic condition between 10 and 19 years of age were more likely to be classed as Adversity than those who did not have such records (78.2 vs. 17.1%).

Boys of Black ethnicity were more likely to be classified into the Adversity group (37.2%) than boys in other ethnic groups (e.g., White: 27.7%). Like girls, the one quarter of boys with missing ethnicity were least likely to be classed as Adversity (21.2%) (Table 4.4). They were also more likely to be classed as Adversity if living in an area of high deprivation, or if they had a chronic condition.

Table 4.3: Characteristics of adolescent girls whose entire ten years of adolescence (10-19 years old) occurred in 1998-2011

	Girls with emergency admission(s) for injury between 10 and 19 years old, n (row %)			
Characteristics	**Total**	**Adversity**	**Accidents Only**	**Other Causes**
All	144,158 (100.0)	72,805 (50.5)	59,465 (41.2)	11,888 (8.2)
Ethnicity				
White	102,875 (100.0)	53,295 (51.8)	40,765 (39.6)	8,815 (8.6)
Black	2,819 (100.0)	1588 (56.3)	955 (33.9)	276 (9.8)
Asian	3,794 (100.0)	2,243 (59.1)	1,124 (29.6)	427 (11.3)
Mixed	1,439 (100.0)	909 (63.2)	415 (28.8)	115 (8.0)
Other	2,136 (100.0)	1157 (54.2)	782 (36.6)	197 (9.2)
Missing	31,095 (100.0)	13,613 (43.8)	15,424 (49.6)	2,058 (6.6)
Deprivation†				
Least deprived	21,601 (100.0)	9,241 (42.8)	10,324 (47.8)	2,036 (9.4)
2nd least deprived	23,136 (100.0)	10,231 (44.2)	10,867 (47.0)	2,038 (8.8)
Middle quintile	25,179 (100.0)	12,351 (49.1)	10,739 (42.7)	2,089 (8.3)
2nd most deprived	30,466 (100.0)	16,347 (53.7)	11,677 (38.3)	2,442 (8.0)
Most deprived	41,218 (100.0)	23,614 (57.3)	14,823 (36.0)	2,781 (6.7)
Missing	2,558 (100.0)	1,021 (39.9)	1,035 (40.5)	502 (19.6)
Chronic condition**				
Record	78,762 (100.0)	61,616 (78.2)	12,260 (15.6)	4,886 (6.2)
No record	65,396 (100.0)	11,189 (17.1)	47,205 (65.3)	7,002 (10.7)

*Grouped by Index of Multiple Deprivation quintiles.
**Any codes from chronic conditions cluster, in records for any admissions at 10-19 years old (cluster available from Appendix C.4)

Table 4.4: Characteristics of adolescent boys whose entire ten years of adolescence (10-19 years old) occurred in 1998-2011

	Boys with emergency admission(s) for injury between 10 and 19 years old, n (row %)			
Characteristics	**Total**	**Adversity**	**Accidents Only**	**Other Causes**
All	258,503 (100.0)	68,403 (26.5)	174,267 (67.4)	15,833 (6.1)
Ethnicity				
White	176,335 (100.0)	48,796 (27.7)	116,669 (66.2)	10,870 (6.2)
Black	5,472 (100.0)	2033 (37.2)	3048 (55.7)	391 (7.1)
Asian	6,843 (100.0)	2,010 (29.4)	4,150 (60.6)	683 (10.0)
Mixed	2,247 (100.0)	754 (33.6)	1331 (59.2)	162 (7.2)
Other	3,847 (100.0)	1265 (32.9)	2270 (59.0)	312 (8.1)
Missing	63,759 (100.0)	13,545 (21.2)	46,799 (73.4)	3,415 (5.4)
Deprivation†				
Least deprived	42,339 (100.0)	7,907 (18.7)	31,564 (74.6)	2,868 (6.8)
2nd least deprived	42,722 (100.0)	8,942 (20.9)	31,105 (72.8)	2,675 (6.3)
Middle quintile	45,622 (100.0)	11,081 (24.3)	31,642 (69.4)	2,899 (6.4)
2nd most deprived	52,348 (100.0)	15,309 (29.2)	33,990 (64.9)	3,049 (5.8)
Most deprived	70,449 (100.0)	23,594 (33.5)	43,199 (61.3)	3,656 (5.2)
Missing	5,023 (100.0)	1,570 (31.3)	2,767 (55.1)	686 (13.7)
Chronic condition**				
Record	72,625 (100.0)	38,442 (52.9)	28,846 (39.7)	5,337 (7.3)
No record	185,878 (100.0)	29,961 (16.1)	145,421 (78.2)	10,496 (5.6)

*Grouped by Index of Multiple Deprivation quintiles.
**Any codes from chronic conditions cluster, in records for any admissions at 10-19 years old (cluster available from Appendix C.4)

Prevalence by age-group and age-year

Table 4.5 shows the population prevalence of the Adversity, Accidents Only and Other Causes groups, by age-group. The prevalence of Adversity in each of these age-groups was lower than for 10-19 year olds as a whole (e.g., 1.2% of 10-14 year old girls in the general population were classed as Adversity compared with 4.6% of 10-19 year olds). This difference is due to the smaller number of admissions on which the classification of Adversity could be based.

Girls were most likely to be classed as Adversity at 15-17 years old compared to other age-groups. Boys were most likely to be classed as Adversity at 18-19 years old. Both girls and boys were most likely to be classed as Accidents Only at 10-14 years old. With regards to 10-19 year olds, self-inflicted and drug/alcohol-related injury were the most common types of adversity-related injury for girls in all age-groups, and violent and drug/alcohol-related injury were the most common for boys.

Plots of prevalence by age-year display similar patterns as seen for age-groups (Figure 4.5). The peak age for Adversity was 15 years old in girls and 19 years old in boys (Figure 4.5). These plots also show that in girls the prevalence of an emergency admission for injury with age was driven by prevalence of Adversity, whereas in boys the prevalence was driven by that of the Accidents Only group in younger years (around 10 to 14 years old), and by prevalence of Adversity in older years.

Table 4.5: Population prevalence (%) of emergency admission(s) for injury among 10-19 year olds in England (1998-2011), by sex and types of injury within age periods*

	Girls			Boys		
Adolescent group† **Types of injury**	**10-14y**	**15-17y**	**18-19y**	**10-14y**	**15-17y**	**18-19y**
All	4.10	3.26	2.19	7.32	5.07	3.85
Adversity	1.24	2.12	1.33	0.67	1.46	1.75
Any violent injury	0.10	0.15	0.11	0.28	0.73	0.83
Any self-inflicted injury	0.78	1.46	0.92	0.17	0.39	0.48
Any drug/alcohol-related injury	1.11	1.96	1.22	0.38	0.81	1.08
Accidents Only	2.22	0.80	0.58	5.89	3.11	2.17
Other Causes	0.45	0.33	0.28	0.76	0.50	0.39

Data are presented as population prevalence (%).
Due to large denominators, confidence intervals for population prevalence were too narrow to provide any meaningful interpretation and so are not shown.
*Each adolescent classified by all adversity/accidents seen at any emergency injury admission(s) at 10-19 years, 10-14 years, 15-17 years and 18-19 years, respectively.

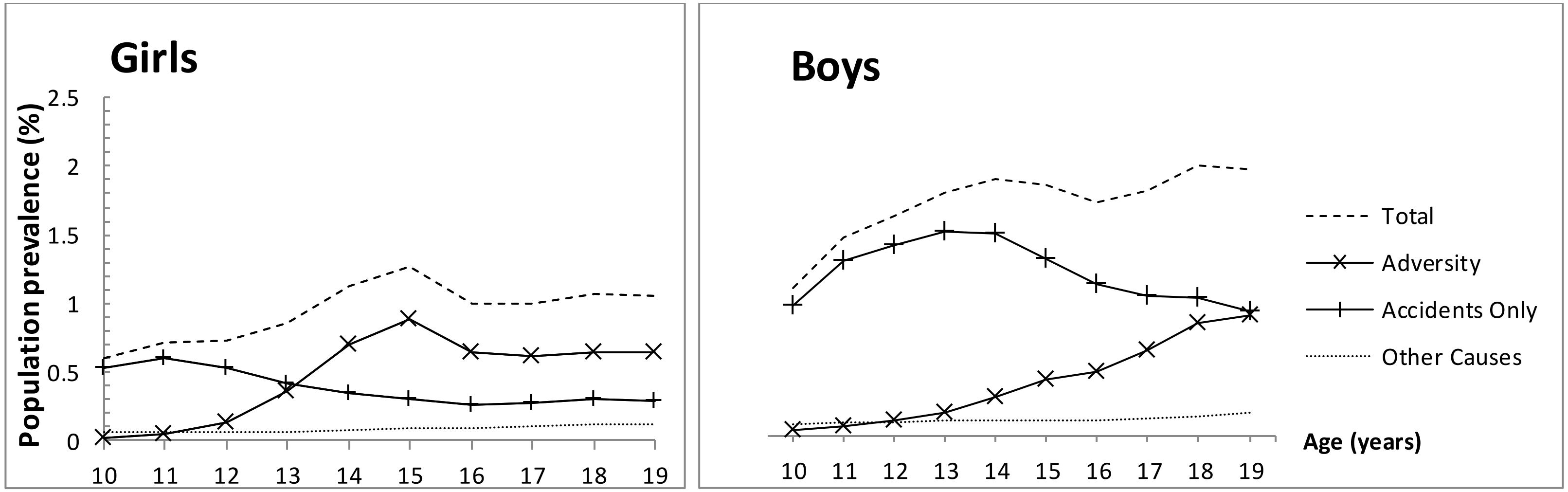


Figure 4.5: Population prevalence of emergency admission(s) for injury, by types of injury within each age year and sex

V = Violent injury; SI = Self-inflicted injury; DA = Drug/alcohol-related injury
Denominators derived from ONS mid-year population estimates for England. Each adolescent classified by all adversity/accidents recorded at any emergency admission(s) for injury within each year of age.

Numbers of admissions

Amongst girls, those in the Adversity group contributed a greater total number of admissions than those in the Accidents Only group (177,972 vs. 111,324) (Table 4.6). Among boys, there were over twice as many admissions in the Accidents Only group compared to the Adversity group (281,171 vs. 128,278). The majority of admissions for girls and boys in the Adversity and Accidents Only groups were emergency admissions, particularly for injury (e.g., girls, non-injury: 26.9%, injury: 54.7%). Half of the 60,000-70,000 admissions (each) for girls and boys in the Other Causes group were non-emergency and non-injury.

Individual girls and boys in the Adversity group contributed disproportionately to the total number of admissions for this group, compared to girls and boys in the Accidents Only group. A higher proportion of adolescents in the Adversity group had two or more admissions between 10 and 19 years of age (girls: 46.2%, boys: 35.2%), compared with adolescents in the Accidents Only group (girls 33.5%; boys: 28.9%) (Figure 4.6). These relative differences were even starker in the case of emergency admissions for injury (girls 17.3 vs. 4.7%, boys 16.5 vs. 7.4%) (Figure 4.7).

Table 4.6: Total number of admissions at 10-19 years old for adolescents in the Adversity and Accidents Only groups

Adolescent group	Number of adolescents	Number of admissions, n (row %)				
		Total	Non-emergency		Emergency	
			Injury	Non-injury	Injury	Non-injury
Girls						
Adversity	72,805	177,972 (100.0)	2,203 (1.2)	30,465 (17.1)	97,356 (54.7)	47,948 (26.9)
Accidents Only	59,465	111,324 (100.0)	2,463 (2.2)	23,992 (21.6)	63,169 (56.7)	21,700 (19.5)
Other Causes	11,888	63,598 (100.0)	2,426 (3.8)	31,991 (50.3)	13,645 (21.5)	15,536 (24.4)
Boys						
Adversity	68,403	128,278 (100.0)	3,845 (3.0)	18,286 (14.3)	85,696 (66.8)	20,451 (15.9)
Accidents Only	174,267	281,171 (100.0)	9,641 (3.4)	48,389 (17.2)	190,565 (67.8)	32,576 (11.6)
Other Causes	15,883	68,032 (100.0)	3,148 (4.6)	33,431 (49.1)	17,782 (26.1)	13,671 (20.1)

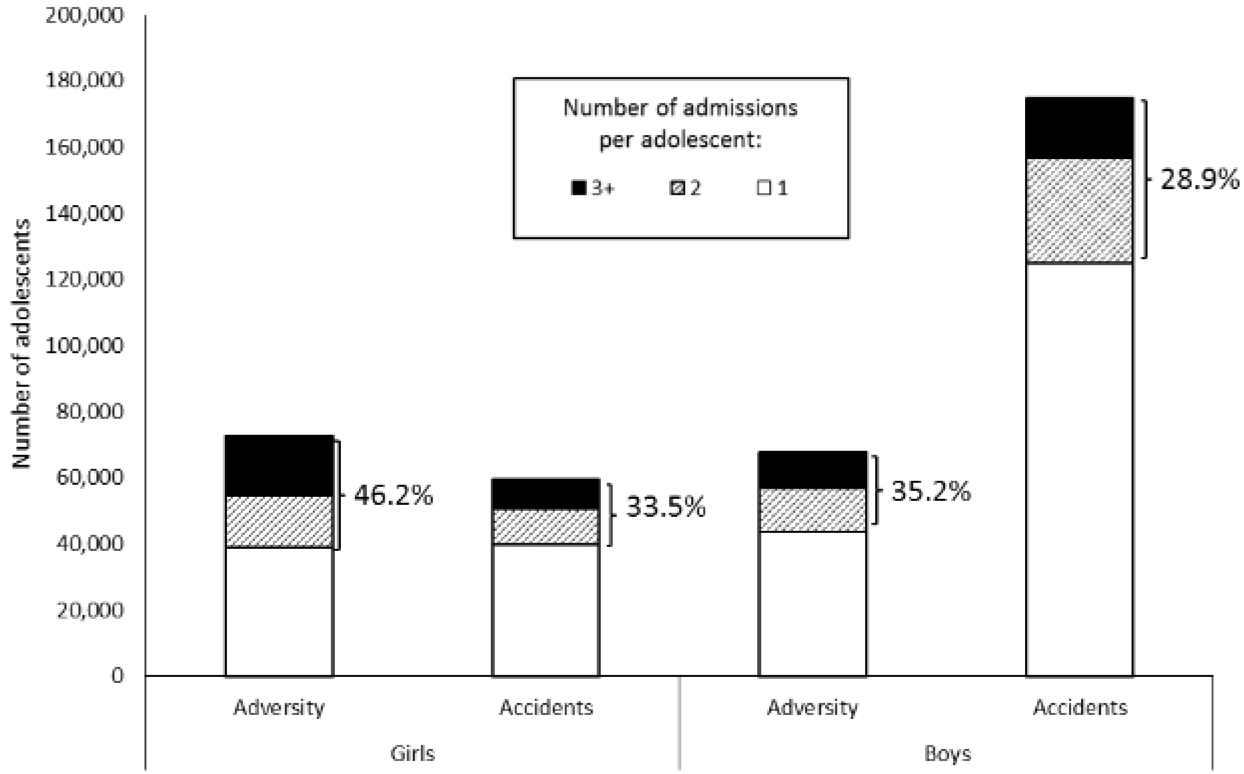


Figure 4.6: Numbers of adolescents who had 1, 2 and 3+ admissions between 10 and 19 years old, by Adversity and Accidents Only groups and sex

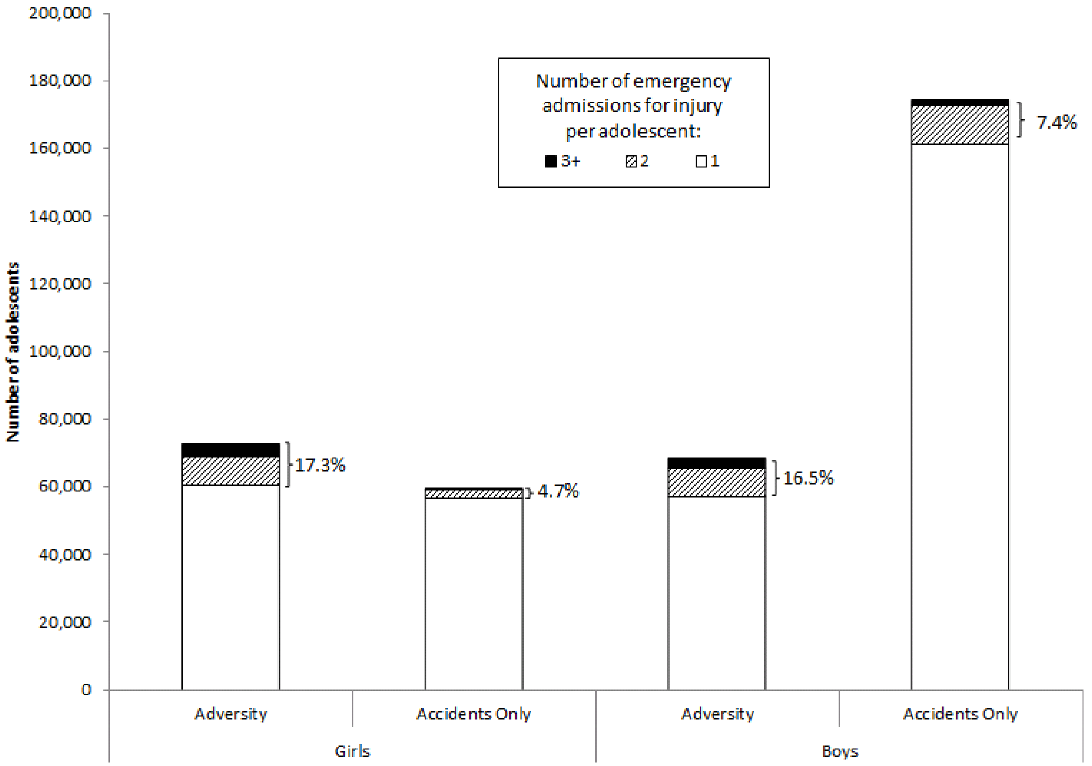


Figure 4.7: Numbers of adolescents who had 1, 2 and 3+ emergency admissions for injury between 10 and 19 years old, by Adversity and Accidents Only groups and sex

4.4.2 Objective 2: Proportions of adolescents with violent, self-inflicted, and drug/alcohol-related injury

Figure 4.8 shows that among girls in the Adversity group, 72.6% were exposed to multiple types of adversity-related injury between 10 and 19 years old (sum of overlaps in Venn diagram = 1.2% + 0.2% + 69.2% + 2.0%), compared with 38.4% of boys in the Adversity group (8.8% + 2.4% + 24.8% + 2.4%). The most common combination of different types of adversity-related injury was self-inflicted and drug/alcohol-related injury (girls: 69.2%, i.e., most of the 72.6%; boys: 24.8%).

Different types of adversity-related injury at the same admission

For most of the adolescents who were exposed to multiple types of adversity, the combination of types was recorded at the same admission, as shown in the table in Appendix E.1. For example, among the 130 adolescent girls in the violent and self-inflicted injury sub-group, 64.6% had both violent and self-inflicted injury recorded simultaneously in at least one emergency admission for injury. Adolescents in the Adversity group also often came in with emergency admissions for accident-related injury only, or other types of injury (Appendix E.2).

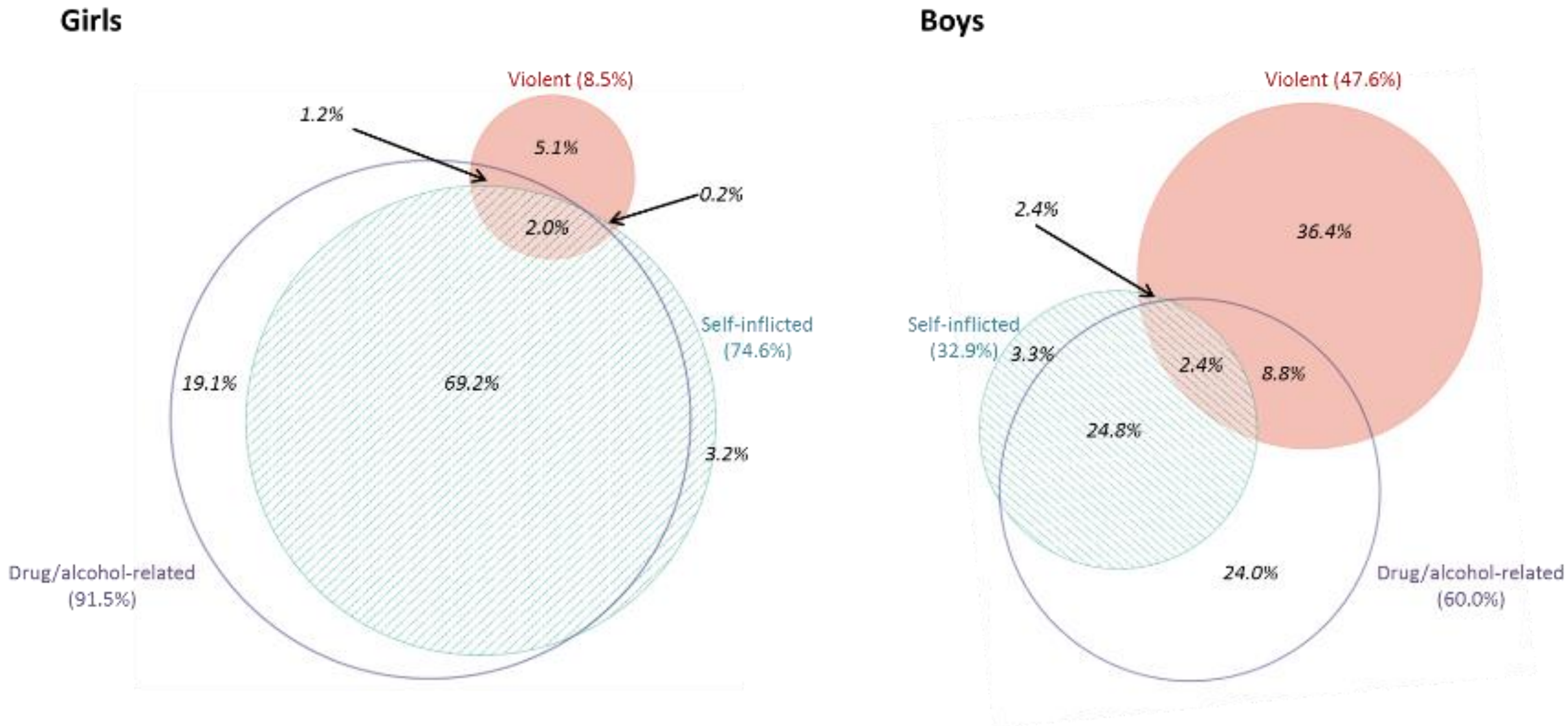


Figure 4.8: Distribution of types of adversity-related injury at adolescents' emergency admissions to hospital between ages 10 and 19

Prevalence of multiple types of adversity-related injury, by age

Figure 4.9 shows the prevalence of combinations of different types of adversity-related injury, by age-year. These plots show that the peak age for Adversity at 15 years old in girls, shown in Figure 4.5, was driven by the prevalence of specifically self-inflicted and drug/alcohol-related injury. The peak age for Adversity in boys in Figure 4.5 (at age 19 years) was driven by the prevalence of admissions for violent injury only, followed by admissions for self-inflicted and drug/alcohol-related injury, and admissions for drug/alcohol-related injury, only.

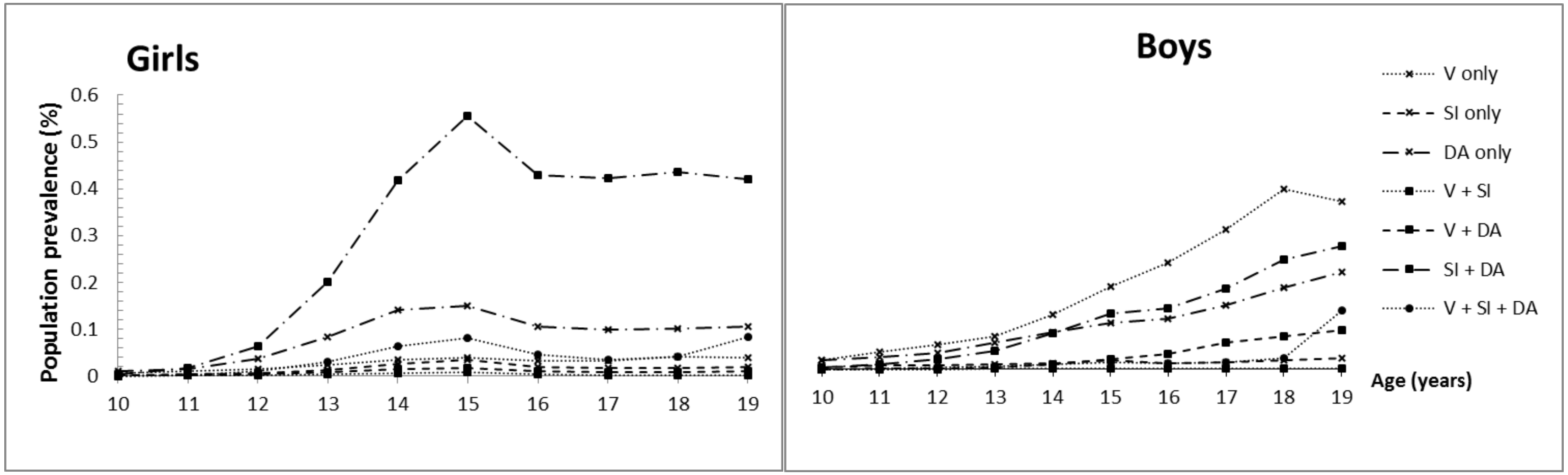


Figure 4.9: Population prevalence of emergency admission(s) for injury, by combination of types of adversity-related injury within each age year and sex

V = Violent injury; SI = Self-inflicted injury; DA = Drug/alcohol-related injury
Each adolescent classified by all adversity/accidents recorded at any emergency admission(s) for injury within each year of age.

Numbers of admissions

Among Adversity sub-groups, the greatest total number of emergency admissions for injury was accounted for by the 50,404 girls who were admitted with self-inflicted and drug/alcohol-related injuries between 10 and 19 years old (Table 4.7). These girls had 109,051 emergency admissions for injury (i.e., an average of at least two emergency admissions for injury each). For boys, the greatest number was accounted for by those admitted with violence only (39,721 emergency admissions for injury from 24,912 boys) and self-inflicted and drug/alcohol-related injury only (36,646 emergency admissions for injury from 16,391 boys).

Among adolescents in the Adversity group, those who were ever admitted for multiple types of adversity-related injury were more likely to have two or more admissions compared to those only ever admitted with a single type (multiple types, girls: 21%, boys: 24%; single, girls: 7%, boys: 12%) (Table 4.7, Table 4.8), particularly girls and boys with all three types of adversity-related injury (girls: 63.1%, 30.5%). Similar patterns were observed for the proportions of adolescents admitted as an emergency with injury, two or more times. The proportions of adolescents with three or more emergency admissions (injury-related or not), were also greater for those with multiple types of adversity-related injury compared with single.

Table 4.7: Proportion of girls in England (1998-2011) with 1, 2 or 3+ admission(s) between 10 and 19 years old, by type of admission and adolescent injury group

		Admission(s) of any type**			Emergency admission(s) for injury		
Adolescent injury group*	**No. girls**	**1**	**2**	**3+**	**1**	**2**	**3+**
All	144,158	57.6	20.5	22.0	88.6	8.3	3.1
Adversity	72,805	53.8	21.1	25.1	82.7	12.0	5.3
Any violent injury	6,211	49.1	20.7	30.1	77.2	13.9	8.9
Any self-inflicted injury	54,315	51.2	21.5	27.3	79.3	13.9	6.8
Any drug/alcohol-related injury	66,645	53.6	21.1	25.3	81.9	12.5	5.6
Single type	19,924	61.2	19.8	19.0	92.8	6.2	1.0
V only	3,734	58.1	20.4	21.6	92.4	6.3	1.3
SI only	2,296	54.4	20.7	24.9	90.3	8.1	1.6
DA only	13,894	63.2	19.5	17.4	93.3	5.9	0.8
Multiple types	52,881	51.0	21.6	27.4	78.9	14.2	6.9
V + SI	130	42.3	26.2	31.5	70.0	20.8	9.2
V + DA	862	52.2	22.9	24.9	81.9	15.1	3.0
SI + DA	50,404	51.8	21.6	26.6	80.1	13.7	6.3
V + SI + DA	1,485	25.5	19.9	54.5	36.8	31.6	31.5
Accidents Only	59,465	66.5	18.7	14.7	92.6	6.5	0.9
Other Causes	11,888	35.5	25.8	38.8	93.4	5.0	1.6

V = Violent injury, SI = Self-inflicted injury, DA = Drug/alcohol-related injury
* Each adolescent classified by all adversity/accidents seen at any emergency admission(s) for injury between 10 and 19 years old.
** 'Any type' = whether emergency, injury, adversity-related injury (or not).

Table 4.8: Proportion of boys in England (1998-2011) with 1, 2 or 3+ admission(s) between 10 and 19 years old, by type of admission and adolescent injury group

		Admission(s) of any type**			Emergency admission(s) for injury		
Adolescent group*	**No. boys**	**1**	**2**	**3+**	**1**	**2**	**3+**
All	258,503	68.5	18.7	12.9	90.3	8.0	1.8
Adversity	68,403	64.8	19.4	15.8	83.5	12.4	4.1
Any violent injury	32,799	65.6	19.6	14.8	83.2	12.8	4.0
Any self-inflicted injury	21,087	57.0	20.7	22.3	76.7	15.8	7.5
Any drug/alcohol-related injury	41,014	62.9	19.5	17.6	81.1	13.6	5.3
Single type	43,563	55.8	15.2	10.3	71.3	8.3	2.2
V only	24,912	68.3	19.2	12.6	87.1	10.6	2.2
SI only	2,260	62.3	19.8	17.9	87.3	10.4	2.3
DA only	16,391	69.9	17.9	12.2	88.5	9.5	2.1
Multiple types	24,840	58.1	20.7	21.2	76.2	16.4	7.4
V + SI	217	52.1	25.3	22.6	65.9	24.4	9.7
V + DA	6,013	63.6	20.2	16.1	78.7	17.5	5.1
SI + DA	16,953	58.6	20.6	20.8	78.8	14.9	6.3
V + SI + DA	1,657	34.1	22.4	43.5	42.0	31.2	26.8
Accidents Only	174,267	71.4	18.1	10.5	92.6	6.5	0.9
Other Causes	15,833	51.5	22.1	26.3	93.4	5.0	1.6

V = Violent injury, SI = Self-inflicted injury, DA = Drug/alcohol-related injury
* Each adolescent classified by all adversity/accidents seen at any emergency admission(s) for injury between 10 and 19 years old.
** 'Any type' = whether emergency, injury, adversity-related injury (or not).

4.4.3 Sensitivity analyses

There was a moderate effect on prevalence when using only the primary field of diagnosis to define adversity-related and accident-related injury (rather than all available fields [up to 20]): 10,317 (2.6%) fewer adolescents were admitted as an emergency with injury according to the new definition. The prevalence of adversity-related injury was even more sensitive to whether the primary field or all fields were used: 59,109 fewer adolescents were defined as having been admitted with adversity-related injury. This translated to a decrease of estimated prevalence from 4.3 per 100 population being admitted with adversity-related injury between 10 and 19 years of age, to 2.5 per 100.

When the ICD-10 code Z91.5 (‘personal history of self-harm’) was excluded from the coding cluster for self-inflicted injury, the number of adolescents who were classified as having been admitted as an emergency with self-inflicted injury decreased from to 75,399 to 73,900 (i.e., a decrease of 1%).

4.5 Discussion

In this study, it was estimated that approximately 1 in 25 adolescents in England had an emergency admission for adversity-related injury between 1997 and 2011. We now also know that the prevalence of an emergency admission for adversity-related injury is likely to be higher for boys than girls, and for older adolescents. For both girls and boys, the most common type of adversity-related injury was drug/alcohol-related injury (particularly at 18-19 years old), which was largely accounted for by illicit drug use in girls, and illicit drug use and alcohol misuse in boys. Among adolescents admitted with adversity-related injury in this study, nearly three quarters of girls and over one quarter of boys were exposed to multiple types (the most common combination being self-inflicted and drug/alcohol-related injury, which were often present at the same admission).

Adolescents admitted with adversity-related injury were more likely to be admitted twice or more times between 10 and 19 years old, particularly for injury. This may be explained by higher levels of psychosocial need leading to repeat incidences of injury.

4.5.1 Strengths and limitations

The main strength of this study is that it captured nearly the entire population of interest. That is, all adolescents admitted to hospital in England as an emergency, with adversity-related injury. Analysis of the large HES dataset allowed estimation of the prevalence of three types of adversity and their combinations within the same cohort, by sex and age, and to study associations with other characteristics such as ethnicity. Longitudinal linkage of admissions permitted the study of the entire ten years of adolescence, and allowed us to distinguish between types of adversity that co-occurred during adolescence or at the same admission.

Prevalence estimates were not substantially sensitive to possible variability around estimated population counts (which were used as denominator values). For example, for the prevalence of an emergency admission for injury between 10 and 19 years old, the estimated prevalence among girls was 8.66% (Table 4.3). If the population denominator value (1,665,104) was increased and decreased by 30,000 (the maximum likely change in population count if we cannot assume balanced migration levels; see 3.4.3), this estimated prevalence would have been 8.50% and 8.82%, respectively.

The principal limitation of this study is the only moderate sensitivity of ICD-10 codes for picking up adversity-related injury (see Section 3.3.6). This is likely to mean that the estimated prevalence of adversity-related injury was underestimated in this study, and overestimated for accident-related injury.

In the case of self-inflicted injury, I included self-harm codes for determined, but not undetermined intent (Y10-Y34), the latter has been used in previous research in self-harm (214). These codes for undetermined intent were included in the violence cluster (Y20-Y34) and drug/alcohol-related injury cluster (Y10-Y19), which were purposefully mutually exclusive from each other and other clusters. This may mean that the relative prevalence of different types of adversity-related injury are, in reality, slightly different to the estimates of the current study. However, the prevalence of adversity-related injury (as a whole) would not have been affected.

Some adolescents were not included in the cohort for this study because they would not have been observed for the entirety of their adolescence (e.g., those who were 10 years old in 2003 and therefore turned 19 years old beyond the dataset). The prevalence of adversity-related injury for the study cohort may have altered for these adolescents. We recently reported the rates of emergency admissions of 10-18 year olds to hospitals in England, for adversity-related injury (215). We found that this incidence decreased over time for all 10-15 year olds and 16-18 year old boys, but increased for 16-18 year old girls, and that this increase was apparent for all three types of adversity-related injury. Therefore, it is possible that the prevalence of emergency admissions for adversity-related injury, for adolescents who were

10 years old beyond 2002, may be slightly different to the prevalence estimated in the current study.

4.5.2 Comparisons with other studies

To my knowledge, there were no published studies with which to compare the estimated 4% prevalence of emergency admissions for adversity-related injury (Section 1.4). The estimated prevalence of admissions for violent injury (girls: 760 per 100,000, boys: 2,200 per 100,000), was higher than that reported for assault-related injury in a previous study by Bellis *et al*, which used HES data from 2004-2009 (up to 120 per 100,000 girls and up to 700 per 100,000 boys) (51). This difference is likely due to the broader coding clusters which I used for violence. Estimated prevalence of admissions for self-inflicted or drug/alcohol-related injury in the current study aligned well with those from general population studies (34, 213). For example, Hawton *et al* showed that approximately 1.46% of 15-16 year olds in the general population in England attend hospital for self-harm (34), and other research shows that a minority would have been admitted (216). In the current study, 0.32-0.42% of adolescents in the general population had an emergency admission for self-inflicted injury at ages 15-16 (data not shown).

The ratio of self-inflicted injury between girls and boys (girls 54,315: boys 21,087; Table 4.1), was similar to that in a study of 50 14-16 year olds who presented at hospital with self-inflicted injury but who were not necessarily admitted (216). Historically, higher rates of drug/alcohol-related have been reported in boys compared to girls in the general adolescent population (213). However in the current study of admitted adolescents, more girls than boys were admitted with drug/alcohol-related injury (girls 66,645: boys 41,014), for all age groups (Table 4.1). This contrast between drug/alcohol-related injury in the general population and for admitted adolescents could indicate that girls exposed to drug/alcohol misuse are more likely to be injured, present to hospital, or be admitted after presenting to hospital, as a result. Indeed, in the past decade in England, the annual survey of 11-15 year olds, ‘Smoking, drinking and drug use in young people in England’, has observed the gap between girls and boys to be closing (35, 217). Similar findings of converging prevalence of drug/alcohol-related injury between girls and boys have been reported for 11-14 year olds in the US (218).

It is difficult to compare the prevalence of combinations of adversity-related injury (other than specifically self-inflicted with drug/alcohol-related injury) in the current study with other studies in the literature for two reasons: firstly, because multiple types are rarely studied in hospital-based populations, and secondly, because the definition of drug/alcohol misuse varies greatly. For example, a cohort study of 11-18 year old school children in England and Wales prior to 2006 reported the proportion who engaged in violence and drank alcohol (6), but fighting and drinking were categorised on five different levels for each variable.

4.5.3 Implications of findings

This study has shown that a non-negligible proportion of adolescents are admitted to hospital as an emergency with adversity-related injury, who may be targeted with preventative strategies at discharge. Violent injury accounted for a large proportion of adversity-related injury, and thus national clinical guidelines for management of adolescents seen with violent injury should exist, as they do for self-inflicted and drug/alcohol-related injury (see Table 1.3).

Adolescents admitted to hospital with adversity-related injury are often exposed to multiple types of adversity, which highlights the importance of psychosocial assessment before discharge, to capture other vulnerabilities for these adolescents, not just that of the presenting injury. Adolescents admitted with adversity-related injury account for a large proportion of all emergency admissions for injury in this age-group (29.1 to 50.0%) and are more likely to have recurrent admissions compared to adolescents admitted with accident-related injury. Interventions for adolescents admitted with adversity-related injury that reduce their risks of harm after discharge, may reduce not only suffering for the adolescent in question but burden on health services through numbers of admissions. These numbers do not account for temporality. That is, the 'extra' admissions could have taken place before the admission for adversity-related injury that placed the adolescent in question in the Adversity group. Further work in Chapter 5 will assess the risks of *re*-admissions (as well as death) following an index admission for adversity-related injury. The total numbers of admissions presented in this chapter provides a base comparison for this further work.

Chapter 5 Statistical methods for estimating risks of harm following admissions for adversity-related and accident-related injury

5.1 Chapter summary

This chapter describes statistical methods for analysing time-to-event (or 'survival') data, which were applied or considered to address Objectives 3 to 5 of this thesis.

In Section 5.4, I describe how I used the cumulative failure function to estimate absolute risks of death and emergency re-admission in the ten years after discharge from emergency admissions for adversity-related injury during adolescence (Objective 3). The cumulative failure function is mathematically related to the failure, survival, hazard and cumulative hazard functions, which are also described (Table 5.1).

In Section 5.5, I describe proportional hazards (PH; or 'Cox') models, which were fitted in this thesis to compare risks of death and emergency re-admission following adversity-related injury with those following accident-related injury (Objective 4). The PH model does not assume a form for the baseline hazard function. Parametric time-to-event models, which do assume a form for the baseline hazard were also considered, and are described in this section.

In Section 5.1, I describe 'competing risks' methods, which were used in this thesis to estimate risks of deaths through different causes (Objective 5). I estimated cause-specific risks of death as cumulative incidence functions, and employed Fine & Gray models to adjust these risks for other covariates. I also considered estimating cause-specific risks by fitting cumulative *failure* functions and semi-parametric PH models whilst assuming other competing events to be censored.

In Sections 5.7 and 5.8, I describe methods used and considered to deal with two methodological issues that arose due to the multi-level structure of the study design and data: 1) the clustering of multiple ‘index’ emergency admissions for injury for the same adolescent, and 2) the correlation between times to emergency re-admissions following an index emergency admission for injury, when an adolescent has multiple emergency re-admissions.

In Section 5.9, I describe model statistics that were used to check goodness-of-fit of time-to-event models (e.g., Cox-Snell residual plots).

5.2 Introduction

Objectives 3 to 5 of this thesis were to:

3. estimate absolute risks of death and emergency re-admission within ten years following emergency admissions for (adversity-related or accident-related) injury during adolescence, by sex, age and other demographic factors;
4. compare these risks following adversity-related injury with those following emergency admissions for accident-related injury;
5. estimate and compare risks of deaths following adversity-related and accident-related injury, by cause of death.

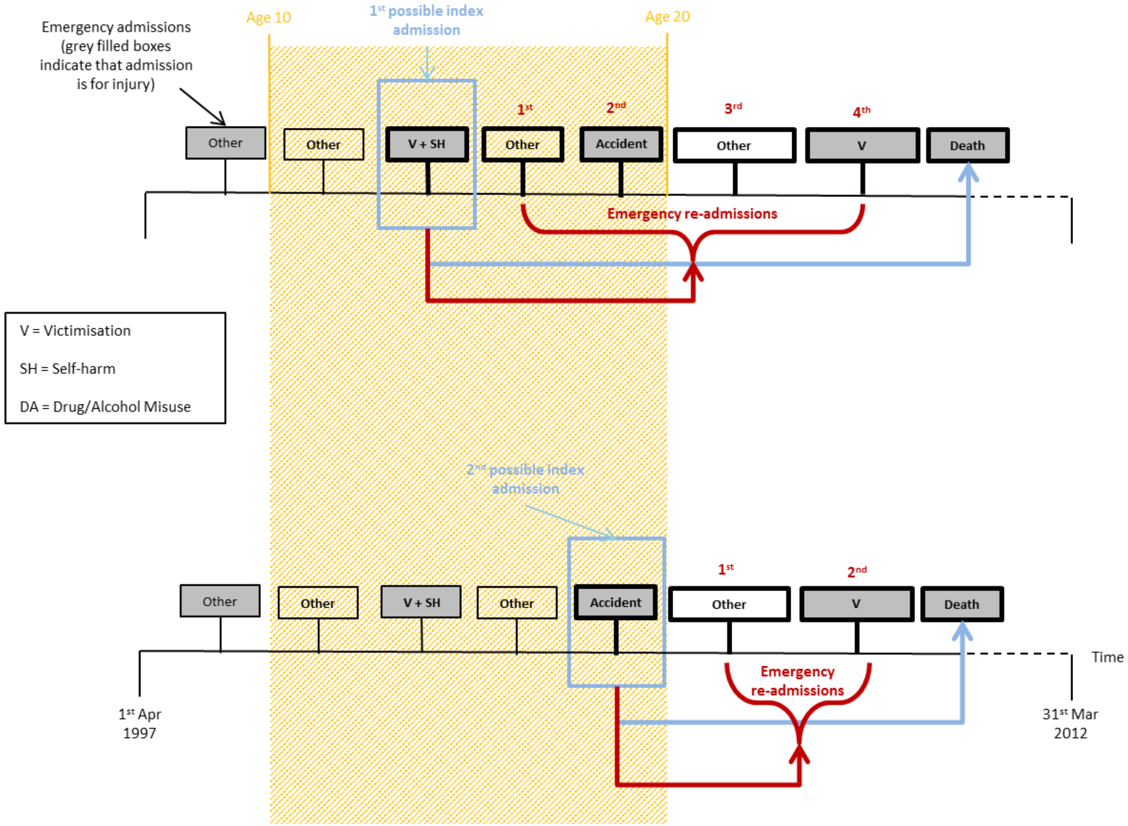
To meet these objectives, I carried out two separate studies: Study II addressed Objectives 3 and 4 and is described in detail in Chapter 6; Study III addressed Objective 5 and is described in Chapter 7. In both studies, I defined an index emergency admission for adversity-related (or accident-related) injury for each adolescent, and used time-to-event ('survival') statistical methods to estimate risks of outcomes in the next ten years.

Due to the study design (Figure 5.1), there were two methodological issues that needed to be taken into account in analyses. First, each adolescent could have more than one emergency admission for injury (adversity-related or accident-related) to be defined as the index (illustrated in Figure 5.1 in blue). Second, each adolescent could have recurrent (more than one) emergency re-admissions following each index admission (illustrated in Figure 5.1 in red).

In the current chapter, I describe methods that I used in Studies II and III, to address both Objectives 3 to 5 and the above two methodological issues. I also briefly discuss alternative methods that I considered (but did not adopt).

Throughout this chapter I illustrate methods using the example of estimating the risk of death following the first emergency admission for adversity-related injury during adolescence, for girls in the extract of HES-ONS data (this subset of adolescents are described in Appendix F). To assess models fitted for this example, I compared their Akaike's Information Criteria (AIC) (219). Unlike several other test statistics for comparing models (e.g., comparing deviance or likelihoods) (220), the AIC does not assume a common structure between models (i.e., nested models). This property was important, as models that were being compared could be structurally very different.

All mathematical notation in this chapter are defined on first mention. A glossary of notation is provided at the beginning of this thesis.



*In interest of data security, this is not a true trajectory for an adolescent in the HES-ONS dataset, but is based on true trajectories.

Figure 5.1: Hypothetical trajectory of an adolescent's emergency admissions*, to illustrate multi-level nature

5.3 Why time-to-event methods?

The outcomes of interest for this thesis were deaths and emergency re-admissions following discharge from an index emergency admission for injury, during adolescence (a binary event).

Traditional statistical methods (e.g. linear or logistic regressions) are often not validly applicable to time-to-event data (e.g., times to deaths or re-admissions). Times to events are often not Normally distributed, as Figure 5.2 demonstrates. This figure shows the times to emergency re-admissions following the first emergency admission for injury, for the example of adolescent girls. These times were extremely positively skewed, and remained skewed even after applying a log transformation (which can be used to render data Normally distributed; not shown). Furthermore, events are typically 'censored'. That is, it is possible that these events are not observed before the end of the study. In the example of adolescent girls, the majority were still alive at the end of the study period (by 30 years old or 31st March 2012). Regular linear or logistic regression models neither have their fundamental assumption (that model residuals are Normally distributed) met (221), or take censoring into account. Therefore, these models produce biased estimates of risk and of average times to events in time-to-event data.

Time-to-event methods take the different lengths of follow-up per individual (induced by death or censoring) into account, by altering the 'risk-set' (the group of individuals on which analyses is carried out) at each time-point.

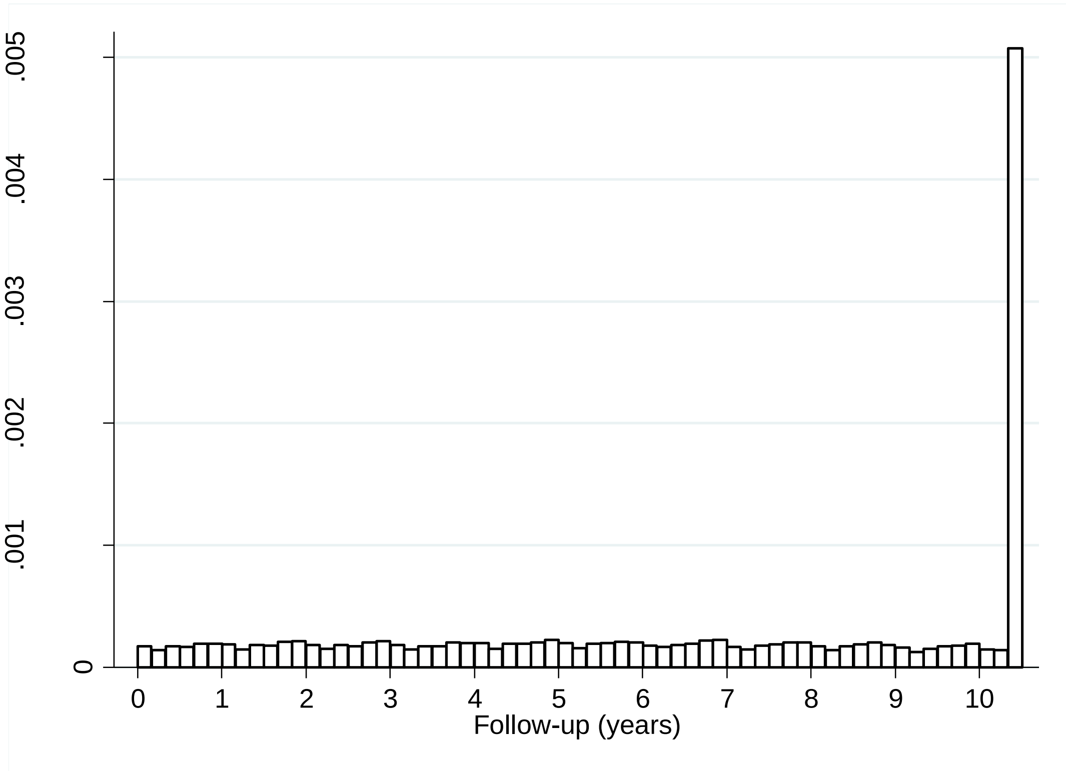


Figure 5.2: Distribution of times to events or censoring (example of adolescent girls)

5.4 Methods for estimating risks of future harm (Objective 3)

In Study II, I estimated absolute risks of death and emergency re-admission following an index admission for adversity-related (or accident-related) injury during adolescence using Kaplan-Meier estimates of the cumulative failure function (referred to as the 'cumulative risk'). I plotted these estimates over time, and presented explicit risk values for specific time-points (1, 5 and 10 years), to allow comparison with estimates from previous studies (181, 184, 185, 222, 223). I employed the cumulative failure function as it could be easily interpreted by clinicians, researchers and policymakers. Other time-to-event functions are discussed in Section 5.4.1. I derived KM estimates of cumulative failure functions, as I considered these estimates to be more conservative than the others available. There were several different formula for these functions, which are discussed in Section 5.4.2).

5.4.1 The cumulative failure function and other related functions

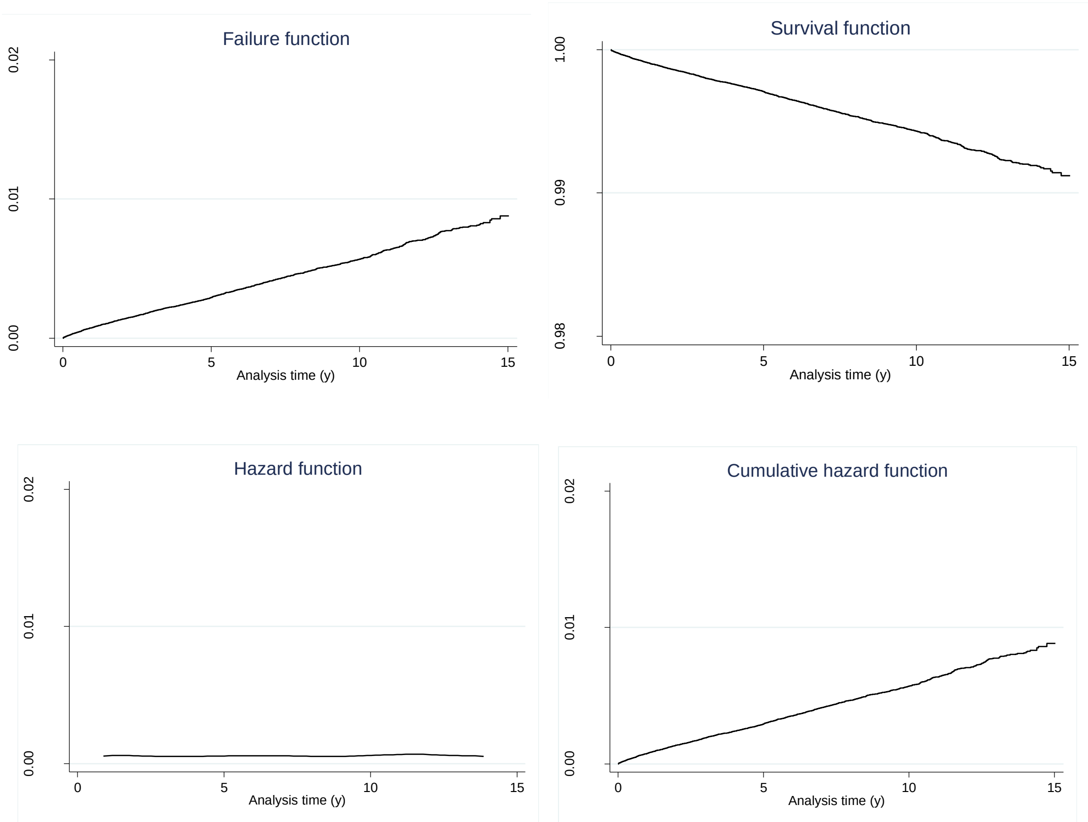
Table 5.1 shows different time-to-event functions and their interpretations. For illustration, Table 5.1 also presents values of these functions for the example of adolescent girls with adversity-related or accident-related injury. The cumulative failure function $F(t_j)$ is the probability that an individual has an event after $t = 0$ and up to (and not including) $t = t_j$. If the event in the example is death, $F(10) = 0.0057$ (Table 5.1). Therefore, approximately 0.57% (or 5.7 per 1,000) of adolescent girls died by ten years following an emergency admission for adversity-related (or accident-related) injury. Figure 5.3 shows the functions in Table 5.1 plotted over time. The cumulative failure function, $F(t)$, consistently increases with time and therefore its 'opposite', the survival function $S(t)$ (i.e., the probability that an individual is alive by time t), consistently decreases with time. The hazard function, $h(t)$, is the event rate per unit time. In Figure 5.3, $h(t)$ is constant with time, and thus the rate at which adolescent girls die does not change with time. This is also indicated by the cumulative hazard, $H(t)$, which consistently increases with time.

Table 5.1 also shows that the failure, hazard and survival functions (and their counterparts) are all mathematically related to each other. Though $F(t)$ was the principal function used in analyses addressing Objective 3, hazard and survival functions (and their counterparts, all of which are described in Table 5.1), were also used in these analyses. For example, most time-to-event regression models depend on an assumption about the shape of the hazard function in particular. (e.g., for proportional hazards or parametric models, discussed in Section 5.5).

Table 5.1: Summary of time-to-event functions (formulae and interpretation)

Time-to-event function	Formula	Interpretation	Example*: t = 10
Probability density (pdf)	$f(t) = P(T = t)$	Probability that an individual has the event at time t.	0.0006
Cumulative density (cdf)	$F(t) = P(T < t) = \int_0^t f(u)\,du$	Probability that an individual has the event before time t.	0.0057
Survival	$S(t) = P(T \geq t) = 1 - F(t)$	Probability that an individual survives past time t.	0.9943
Hazard	$h(t) = P(T < t + \Delta \mid T > t) = \frac{f(t)}{S(t)} = -\frac{d}{dt}\{\log S(t)\}$	Probability of having the event in the next unit interval of time, given that the individual has not had the event up to time t.	0.0006
Cumulative hazard	$H(t) = \int_0^t h(u)du = -logS(t)$	Not a probability, but the total risk that has been accumulated up to time t. Interpreted as the number of events expected by time t, if the event is renewable.	0.0024

*Risks of death for adolescent girls admitted as an emergency with adversity- related or accident-related injury, derived from Kaplan-Meier estimate of $S(t)$ to five significant figures.



F(t) = Cumulative density function (derived from Kaplan-Meier estimate of $S[t]$)); $S(t)$ = Survival function (Kaplan-Meier estimate); $h(t)$ = hazard function (derived from Kaplan-Meier estimate of $S[t]$); $H(t)$ = Cumulative hazard function (Nelson-Aalen estimate)

Figure 5.3: Time-to-event functions for time to death (example of adolescent girls with adversity-related or accident-related injury)

5.4.2 Kaplan-Meier, Life-table, and Nelson-Aalen estimates

Time-to-event functions can be estimated non-parametrically using different formulae. KM, life-table, and Nelson-Aalen (NA) estimates of $S(t)$, $h(t)$ and $H(t)$ are summarised in Table 5.2. $F(t)$ can be derived as $1 - S(t)$.

For estimating cumulative risks of death and emergency re-admission in Study II, I used KM estimates of $F(t)$. As described in Table 5.2, life-table estimates must be calculated for time intervals of equal length (i.e., less flexible than KM or NA estimates). NA estimates are mathematically equivalent to or larger than KM estimates. That is, they are less conservative.

Table 5.2 also includes different estimates of $F(t)$ for the example of adolescent girls with adversity-related or accident-related injury, where the event was death. The KM, life-table, and NA estimates for $F(10)$ were similar (KM: 0.0057, life-table: 0.0058, NA: 0.0057). Thus they all indicate a risk of death of approximately 6 per 1,000.

Table 5.2: Formulae and description of life-table, Kaplan-Meier and Nelson-Aalen estimates of time-to-event functions

Type of Survival Function	Description	Survivor and Hazard Function Equations	Notes	Example*: $F(10)$
Kaplan-Meier, $\hat{S}(t)$	Sets a new time interval each time one or more subjects die and uses richer information. Derived from calculating the cumulative probability of survival past each interval.	$\hat{S}(t_i) = \prod_{j=1}^{i}\left(\frac{n_j - d_j}{n'_j}\right)$ $\hat{h}(t_j) = \frac{d_j}{n_j \times \tau_j}$	.	0.0057
Life-table, $S^*(t)$	Proportion of subjects that would be alive at the end of each time interval	$S^*(t_i) = \prod_{j=1}^{i}\left(\frac{n'_j - d_j}{n'_j}\right)$ $n'_j = n_j - (c_j/2)$, number of subjects that could on average possibly die during jth interval after censoring (the 'actuarial assumption'). $h^*(t_j) = \frac{d_j}{(n'_j - \frac{d_j}{2}) \times \tau_j}$ where $\tau_j = t_{j+1} - t_j$	Calculated with intervals of equal length. Census data can be used in this way and therefore this is also known as the 'actuarial estimate'.	0.0058
Nelson-Aalen, $\tilde{S}(t)$	Like $\hat{S}(t)$ also uses individual event times.	$\tilde{H}(t_i) = \sum_{j=1}^{i} \frac{d_j}{n_j}$ $\Rightarrow \tilde{S}(t_i) = \prod_{j=1}^{i} exp\left(\frac{-d_j}{n_j}\right)$	$\hat{S}(t)$ approximates $\tilde{S}(t)$ via the Taylor Expansion (224). $\hat{S}(t) \leq \tilde{S}(t)$. $\tilde{S}(t)$ said to perform better in small samples than $\hat{S}(t)$.	0.0057

Within jth interval: n_j = number of subjects, c_j = number of censored events, d_j = number of events.

*Risks of death for adolescent girls admitted as an emergency with adversity-related or accident-related injury, estimate to five significant figures.

5.5 Methods for comparing risks of harm following adversity-related injury with those following accident-related injury (Objective 4)

In Study II, to compare risks of death and emergency re-admission following an index admission for adversity-related injury with those following accident-related injury, I fitted semi-parametric PH models.

Cumulative risks of outcomes between two groups can be compared through the confidence intervals (CIs) of the estimated cumulative failure function $\hat{F}(t)$, at fixed time-points. The CI for $\hat{F}(t)$ is:

$$CI\left[\hat{F}(t)\right] = \hat{F}(t) \pm z_{\alpha/2} SE\left[\hat{F}(t)\right] = 1 - \prod_{j=1}^{i} \left(\frac{n_j - d_j}{n'_j}\right) \pm z_{\alpha/2} \left[\sum_{j=1}^{k} \frac{d_j}{n_j(n_j - d_j)}\right]^{1/2} \quad [2]$$

where z is the value associated with a 1-α probability within a Z-table (225), and n_j and d_j are as defined in Table 5.2 (footnote). One can validly compare CIs of estimated risks between groups if we can assume that the risk of death following adversity-related injury, $F_{adversity}(t)$, is independent of the risk following accident-related injury, $F_{accident}(t)$. If the CIs of the estimated risks $\hat{F}_{adversity}(t)$, and $\hat{F}_{accident}(t)$ do not overlap, we can conclude that the mean of $F_{adversity}(t)$ and $F_{accident}(t)$ are statistically significantly different. However, the converse is not true (i.e., we cannot conclude that there is no difference when the CIs do overlap) (226). For example, for adolescent girls, $95\%\ CI\left[\hat{F}_{adversity}(10)\right]$= 0.0070 to 0.0081 and $95\%\ CI\left[\hat{F}_{accidents}(10)\right]$ = 0.0035 to 0.0042, and therefore one can conclude that the ten-year risks of death between the two types of injury are statistically significantly different. However, it was clear from analyses for Objectives 1 and 2 of this thesis (Chapter 4; Study I) that sex, age, deprivation, ethnicity, and chronic condition status were not similarly distributed between the two groups. Therefore, comparing CIs between adversity-related and accident-related injury would not be comparing 'like with like'.

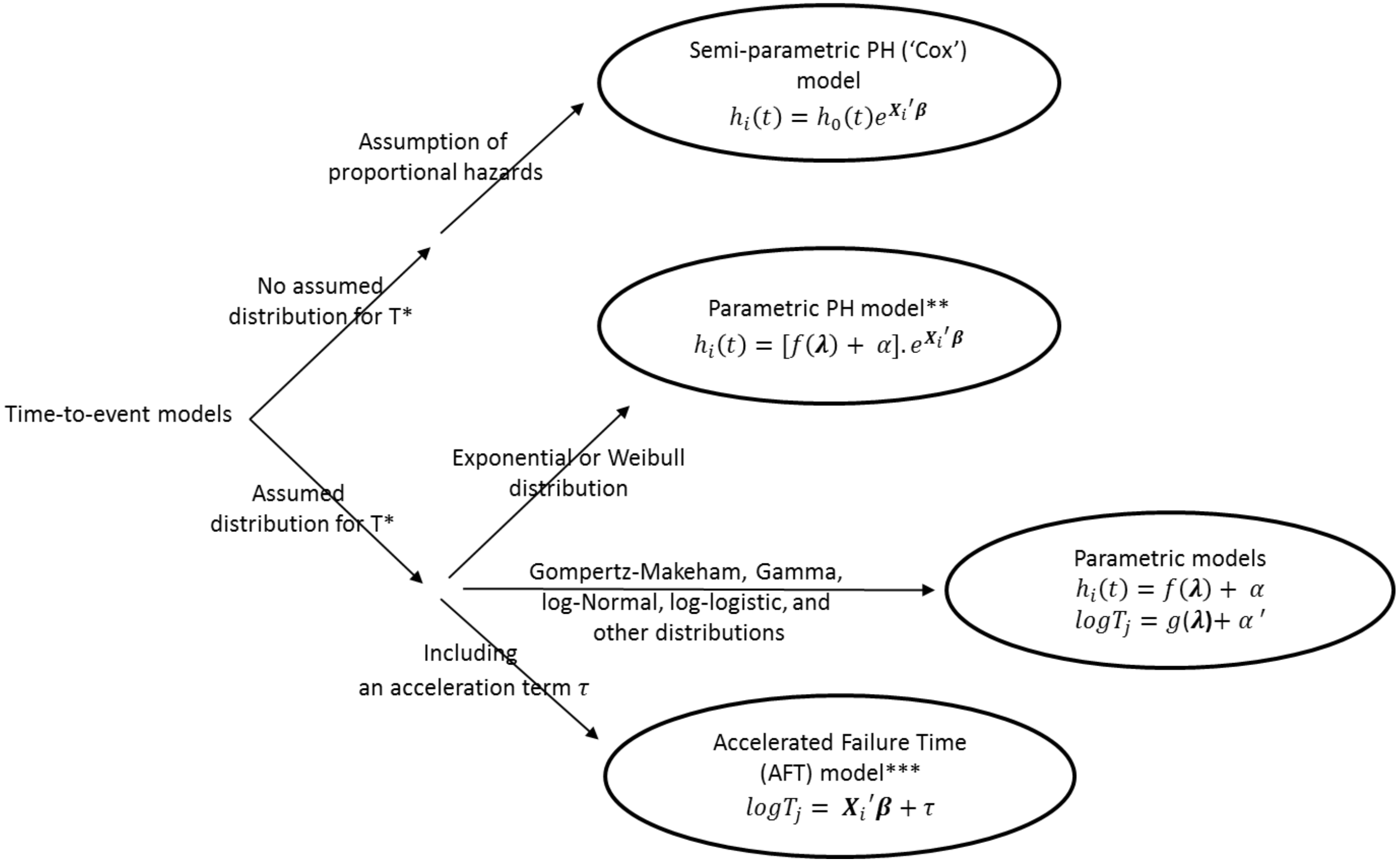
Time-to-event regression models allow comparison of risks between groups, whilst also adjusting for differences in the distribution of the above covariates, that can confound the relationship between adversity-related (versus accident-related) injury and the outcome of death or emergency re-admission.

For the remainder of this section, I discuss the semi-parametric PH model and its assumptions. I describe how in Study II, I:

1) explored PH assumptions using plots of predicted against estimated survival and by testing interaction terms, and

2) accounted for 'tied events' using the average likelihood method.

Alternative models (e.g. flexible parametric models) are also available which are summarised in Figure 5.4 (227). These models can be written either in the hazards or log(time) scale, but most models are typically presented in one scale in particular. For example, the semi-parametric PH model, is usually presented in the research literature in the hazards metric.



PH = Proportional hazards; $\boldsymbol{\lambda}$ are parameters of the assumed distribution, and α and α' are constants; *Therefore an assumed distribution for error term, ε (and baseline hazard if in hazard metric); **Could also be written in the log(T) metric: $logT_j = f(\boldsymbol{\lambda}) + \alpha$; ***Could also be written in the hazards metric: $h_i(t) = [f(\boldsymbol{\lambda}) + \alpha].e^{\boldsymbol{X}_i'\boldsymbol{\beta}+\tau}$

Figure 5.4: Flow diagram illustrating properties of different time-to-event regression models

5.5.1 Semi-parametric proportional hazards models

Model form and estimation

The semi-parametric PH model is the most commonly used regression method for modelling time-to-event data (227). The semi-parametric PH model assumes that a baseline hazard $h_0(t)$ is common across all subjects (i.e., in our case, all adolescents). The hazard for subject i, $h_i(t)$, is modelled as follows:

$$h_i(t) = h_0(t)e^{\boldsymbol{X}_i{}'\boldsymbol{\beta}} \qquad [3]$$

where the covariates $\boldsymbol{X}_i$ can be fixed from baseline (e.g., sex), or be time-varying (e.g., whether currently receiving therapy or not).

As the baseline hazard $h_0(t)$ is assumed to be the same across all subjects, the hazard ratio (HR) for a covariate, $\frac{h(t|X_1=1)}{h(t|X_1=0)}$, represents the multiplicative change in hazard when the covariate increases by one unit. For example, if X_1 represents the sex covariate where 1 = girls and 0 = boys, the HR for girls (versus boys) is $\frac{h_0(t)e^{1 \cdot \beta_1}}{h_0(t)e^{0 \cdot \beta_1}} = e^{\beta_1}$.

The parameter vector $\boldsymbol{\beta}$ can be estimated by assuming that the β_i's are each Normally distributed, and by maximising the partial likelihood (PL) equation (227):

$$PL(\hat{\beta}) = \sum_{i=1}^{n} \int_0^\infty [X_i(t) - \bar{x}(\beta,t)]\ dN_i(t) \qquad [4]$$

where $N_i(t)$ is the number of events occurring in the interval $[t, t + \Delta t)$ and $\bar{x}(\beta,t)$ is a weighted mean over X, for the risk-set at time t:

$$\bar{x}(\boldsymbol{\beta},t) = \frac{\sum Y_i(t)exp[\boldsymbol{X}_i(t)'\boldsymbol{\beta}]\boldsymbol{X}_i(t)}{\sum Y_i(t)exp[\boldsymbol{X}_i(t)'\boldsymbol{\beta}]} \qquad [5]$$

where $Y_i(t)$ = 0 when events are censored at time t, and $Y_i(t)$ = 1 otherwise. A numerical solution to the PL equation is typically obtained via the Newton-Raphson algorithm, with starting values of $\widehat{\boldsymbol{\beta}}$ set to 0 (227). Because the model allows estimation of $\widehat{\boldsymbol{\beta}}$ without specifying a form for $h_0(t)$ but at the same time assuming that the β_i's are each Normally distributed, model [1] is referred to as 'semi-parametric'. Calculation of Var($\widehat{\boldsymbol{\beta}}_i$), which can be used to derive confidence intervals (CIs), is described in Collett, 2003 (224).

When I fitted a semi-parametric PH model in the data for adolescent girls, with adversity-related (versus accident-related) injury as an independent variable, and death as the outcome, $\widehat{\boldsymbol{\beta}}_{adversity}$ was estimated as 0.30. That is, the HR for death for those who had adversity-related injury compared to those who had accident-related injury was $exp(0.30) = 2.01$, interpreted as girls with adversity-related injury having approximately double the risk of death compared to those with accident-related injury.

5.5.2 Model assumptions of the semi-parametric PH model

The semi-parametric model requires two assumptions: First, that the hazards between groups of subjects (e.g., between adolescents admitted with adversity-related injury and those admitted with accident-related injury), are proportional. That is, PH refers to a situation where the relative differences in effect between two groups (represented by the HR, e.g., $\frac{h(t|X_1 = adversity-related)}{h(t|X_1 = accident-related)}$,) are constant with time.

The second assumption is that time is a truly continuous variable, or alternatively put, no events can occur at *exactly* the same time (i.e., they are not 'tied'), an assumption for all time-to-event models. The assumption of 'no ties' can be met if time is recorded to a level small enough to distinguish between all event times.

Assumption 1: Proportional hazards

The semi-parametric PH model has been shown to be robust to violations of the PH assumption (228). However, some extensions of standard semi-parametric PH models were also used in analyses for this thesis (e.g., Fine & Gray's subhazard models, described in Section 5.6.1 and used in Study III). The effect of violations of the PH assumption on results of these extended models, are less known (the reasons for nevertheless employing such models, e.g., competing risks of different causes of death, are discussed in Section 5.6) (229). Therefore, I carried out several tests to ensure that the PH assumption could be met to a reasonable degree.

There are several methods to examine whether the PH assumption has been violated or not, particularly when covariates are discrete. These methods are either graphical or formal tests of fit (230, 231). An advantage of graphical tests for PH is that one can identify particular time intervals on the graph where assumptions are and are not met. However, plots can rarely be used to assess the assumption of PH whilst also taking into the account the effect of additional covariates, as they usually involve comparison of non-parametric estimates (221). In addition, the judgement of graphical tests is subjective. Therefore, I employed both graphical and formal statistical tests to check the PH assumption.

Graphical tests

Graphical tests for the PH assumption include:

1. Plotting the cumulative hazard function (described in Table 5.1) against time (one for each level of the covariate in question) and checking for a constant ratio. The ratio should appear constant if there are PH, since:

$$h_1(t) = \propto \times\ h_0(t)\ \Rightarrow H_1(t) = \propto \times\ H_0(t) \qquad [6]$$

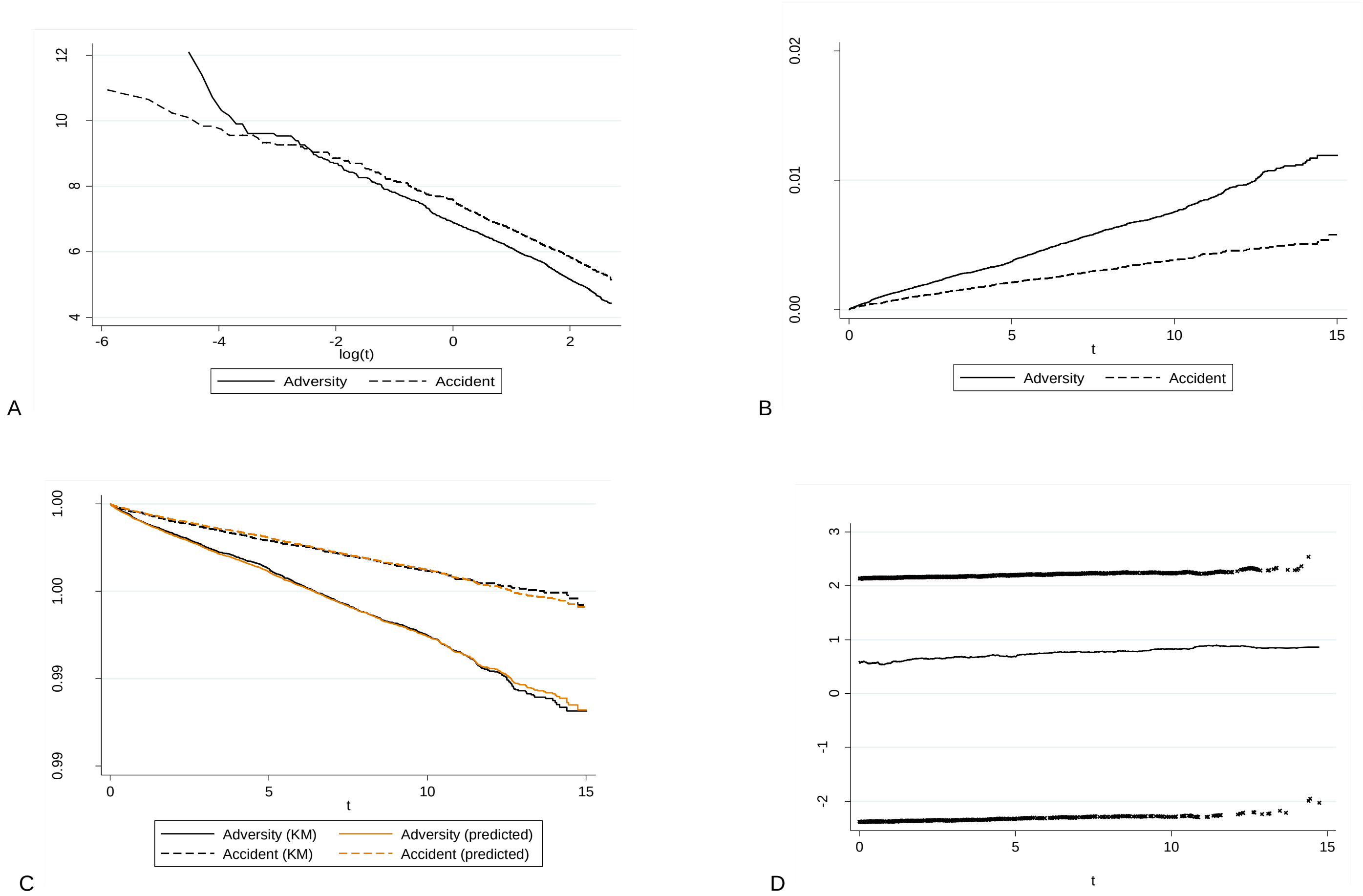
Other variations of this test are also available (e.g., plotting the cumulative hazard functions against each other and checking for a constant slope). Another equivalent model common in the literature is plotting $-\log\{-log(S[t])\}$ against $\log(\mathrm{t})$, where parallel curves denote PH.

2. Plotting the observed KM survival curves (one for each level of the covariate in question) against those predicted by the fitted semi-parametric PH model. Well-aligned curves indicate that the PH assumption is adequately met.
3. Plotting Schoenfeld residuals against time (227). No clear pattern in residuals (i.e. a random scatter) indicates PH.

Chosen method: Plots of predicted vs. estimated survival

When Hess compared the above methods (1. to 3.) on the same sets of data (230), he concluded that generally these methods offer similar power for detecting violation of the PH assumption, except that it is easier to assess by eye whether two curves are parallel, than whether they have a constant ratio or if there is a constant slope. Figure 5.5 illustrates this for the example of adolescent girls. A plot of $-\log\{-log(S[t])\}$ against $\log(\mathrm{t})$ indicates a violation for the PH assumption for $\log(\mathrm{t})$ = -2 (i.e., ~7 months post-discharge), but not thereafter (plot A). This is not as clear from studying the plot of $\mathrm{H(t)}$ against t (plot B). It is also clear from Figure 5.5 that different methods for detecting non-PH do not necessarily agree with each other. The predicted survival curves from a semi-parametric PH model fit those estimated non-parametrically well (plot C), and a plot of Schoenfeld residuals against time are relatively horizontal (plot D), with some negligible deviation around $t \geq 12$. That is, plot A indicates non-PH at different time-points to plot C and D. However, it must be noted that time is on the log-scale in plot A, and therefore the violation is only really indicated until around 7 months post-discharge.

In this thesis, I chose to check the PH assumption in Study II by plotting observed KM survival curves against those predicted by the fitted semi-parametric PH model. I chose this plot in particular because it could be easily interpreted, since plotted on the natural time scale, and non-PH was indicated by an entity that could be judged by eye (i.e., whether predicted and estimated curves aligned). In addition, this plot indicated how well the model fitted the observed data.



Index admission defined as first emergency admission for injury; event is death, independent variable adversity-related (vs. accident-related) injury at index; t = time since discharge from index, in years; S(t) = Estimate of survival at t; KM = Kaplan-Meier estimate; H(t) = Cumulative hazard function

Figure 5.5: Graphical tests of proportional hazards (example of adolescent girls)

Formal tests

Formal statistical tests for the PH assumption include:

1. Fitting ‘piecewise’ models over time, and comparing the estimated coefficients across models (also referred to as the ‘Omnibus test’). If the coefficients are significantly different from each other, this indicates a violation of the PH assumption.
2. Including an interaction term for each covariate with time in the model, and testing whether or not this interaction is significantly different from 0. A significant interaction term indicates a violation of the PH assumption.
3. Testing for a non-zero slope of Schoenfeld residuals (or scaled Schoenfeld residuals) against time (i.e., equivalent to testing for a slope in the Schoenfeld plot, described previously). A non-zero slope indicates a violation of the PH assumption.
4. Score tests where a significant test statistic indicates a violation of the PH assumption (232).

Chosen method: Interaction terms and Schoenfeld residuals

N’gandu compared the above methods (1. to 4.) on simulated sets of data (231), and found that including an interaction term in the model, and Schoenfeld residual tests, had equally good power for detecting violations of the PH assumption, and performed better than piecewise models or the score test. Therefore, alongside a plot of the observed KM against the predicted survival curve, I used these two methods to check the PH assumption in Study II.

The following semi-parametric PH model was fitted to the data for adolescent girls, with a covariate for adversity-related (versus accident-related) injury, as a fixed and time-varying covariate:

$$h_i(t) = h_0(t)e^{\beta_0+\beta_1(x_1=1|adversity)+\beta_2(x_1=1|adversity)t} \quad [7]$$

The results of this model fit are presented in Table 5.3. The HR for the main effect of adversity-related (versus accident-related) injury was 1.68 (95% CI: 1.40 to 2.00). That is, the HR decreased compared to when including a fixed effect only (from 2.01). The HR for the time-varying effect of adversity-related injury (i.e. e^{β_2}) was 1.04 (95% CI: 1.01 to 1.07), evidence that the effect of adversity-related (versus accident-related) injury marginally changed with time.

When the model was fit again, but within each of the time intervals mentioned above (1 to 7, 8 to 11, 12 to 365, 366+ days), the HR for the main effect was substantially different between intervals, and the time-varying effect was still significant within all of these intervals. In this situation, the global HR of 1.68 poorly represented the effect of adversity-related injury within intervals before 366 days, but was relatively close to that for 366 to 5,489 days (1.52). These results indicate that a semi-parametric PH model could be reliably used to compare times to death after adversity-related injury with those after accident-related injury in adolescents alive at one year post-discharge. However, they also show that a more complex model (e.g., one where the effect of adversity-related injury is allowed to vary with time) is required for comparing risks of death before one year.

Table 5.3: Semi-parametric PH model results: main and time-varying effects (example of adolescent girls)

Time interval (days since discharge)	HR for main effect* (95% CI)		HR for time-varying effect* (95% CI)	
(1, 5489)	2.01	(1.81 to 2.24)	Not estimated	
(1, 5489)	1.68	(1.40 to 2.00)	1.04	(1.01 to 1.07)
(1, 7)	0.06	(0.62 to 0.68)	95.60	(42.21 to 216.53)
(8, 11)	Not estimated, only 8 events in this time interval			
(12, 365)	1.05	(0.61 to 1.82)	4.30	(1.49 to 12.4)
(366, 5489)	1.52	(1.21 to 1.91)	1.05	(1.02 to 1.09)

CI = Confidence Interval, HR = Hazard Ratio
*Risks of death for adolescent girls admitted as an emergency with adversity-related (vs. accident-related) injury

Assumption 2: No tied events

In the extract of HES-ONS data, information was recorded to the nearest day, and it was therefore possible for two or more adolescent to have events (observed or censored) on the same day. Therneau and Grambsch have defined more than ten tied events as large enough to substantially bias results (227). More than ten tied events was very likely in Study II, as there were over one million individuals and over four million admissions in the HES-ONS extract (described in Figure 3.6). However, there are several methods available to account for tied events in order to reduce the associated potential bias.

Chosen method: Averaged likelihood

One solution for the presence of tied events is to modify the partial likelihood function used to estimate $\boldsymbol{\beta}$ (see Equation [3]), such that censored observations are treated as having happened just after the event. Therefore, the event itself is not treated as censored. This altered 'exact partial likelihood' is computable (233), but very complex and computationally intensive.

A simple alternative to an altered exact PL is to use an 'averaged likelihood' or Breslow's or Efron's approximations to the exact PL instead (227). These three methods are described in detail in Table 5.4. The three approximations only differ in how the denominator of the PL is calculated. None provided an exactly consistent estimator of $\boldsymbol{\beta}$, and their effects on reducing the potential bias depends on how many ties occurred at event times. In general however, the averaged likelihood gives the most accurate approximation to the altered exact partial likelihood described above, followed by Efron's approximation, followed finally by Breslow's. Therefore, I used the averaged likelihood to account for any tied events when fitting models for Study II.

Table 5.4 shows the results when fitting a semi-parametric PH model in the example of adolescent girls, and using each of the three approximation methods. Results using Breslow and Efron's methods for ties are very similar (HR for adversity-related injury = 2.01 to 2.02), but the AIC is much smaller for the averaged likelihood or Efron's approximation.

Table 5.4: Formulae and description of different approximation methods for handling tied events

			Example*	
Approximation	**Likelihood Equation**	**Notes**	**$h_{adversity}(t)$**	**AIC**
Breslow (234)	$$\prod_{j=1}^{r} \frac{\exp(\boldsymbol{\beta}'\boldsymbol{s}_j)}{\left\{\sum_{\in R(t_j)} \exp(\boldsymbol{\beta}'\boldsymbol{x}_l)\right\}^{d_j}}$$ where $t_j$are the individual time points where either censoring or an event occurs, $j = 1, \ldots J$, $\boldsymbol{\beta}$ is the vector of coefficients of the variables $\boldsymbol{x}$ to be estimated, p = number of covariates, d_j is the number of events at t_j, $R(t_j)$ is the set of individuals at risk at time $t_{j,}$ and $\boldsymbol{s}_j$ is the sum of the covariate values across all individuals who have an event at time t_j.	Adequate approximation when the number of tied events at any one time-point is 'not too large' (233)	2.01	37,280
Efron (235)	$$\prod_{j=1}^{r} \frac{\exp(\boldsymbol{\beta}'\boldsymbol{s}_j)}{\sum_{k=1}^{d_j}\left[\sum_{\in R(t_j)} exp(\boldsymbol{\beta}'\boldsymbol{x}_l) - (k-1)d^{j-1}\sum_{\in D(t_j)} exp(\boldsymbol{\beta}'\boldsymbol{x}_l)\right]}$$ where $D(t_j)$ is the set of individuals who have an event at time t_j. All other notation as for Breslow's approximation.	Gives a closer approximation to the exact partial likelihood than Breslow's (227), and as fast to compute.	2.02	30,685
Averaged likelihood (233)	$$\prod_{j=1}^{r} \frac{\left(\exp(\boldsymbol{\beta}'\boldsymbol{s}_j)\right)}{\sum_{P\in Q(t_j)} \prod_{r=1}^{d_j}\left\{\sum_{\in R(t_j,r)} \exp(\boldsymbol{\beta}'\boldsymbol{x}_l)\right\}}$$ Where $Q(t_j)$ is the set of d_j! permutations of individuals who have an event at time t_j. P is a vector $(p_1, \ldots p_{d_j})$ in $Q(t_j)$ and $R(t_j, r) = R(t_j) - (p_1, \ldots\ p_{r-1})$. All other notation as for Breslow's and Efron's approximations.	Sometimes also referred to as 'exact' method (227), as is done in Stata. Computationally intensive when number of ties is 'too large' at any one time point (233). A closer approximation than Breslow's or Efron's.	2.02	30,429

AIC = Akaike's Information Criterion

*Risks of death for adolescent girls admitted as an emergency with adversity-related (vs. accident-related) injury

5.5.3 Alternative methods

If the assumption of PH cannot be met, an alternative option to the semi-parametric PH model is to fit a parametric model. A parametric model is one where there is an assumed distribution for the time to event, T (Figure 5.4). Common assumed distributions for T are exponential, Weibull, Gompertz-Makeham, Gamma, log-Normal and log-logistic (236). A parametric time-to-event model can provide a more efficient fit to the data compared with a semi-parametric PH model, if the assumed distribution of T is appropriate. An appropriately assumed distribution of a parametric model should usually give similar estimates to a semi-parametric PH model, but with narrower CIs.

Parametric models can be fitted within the hazards metric, just like semi-parametric PH models (i.e., a model as in [1] but with an assumed distribution for T, which translates as an assumed distribution for the baseline hazard $h_0(t)$ or residuals ε). For example, the exponential model assumes that $h_0(t)$ = some constant $\propto$:

$$h_i(t) = = h_0(t)e^{\boldsymbol{X}_i{}'\boldsymbol{\beta}} = \propto e^{\boldsymbol{X}_i{}'\boldsymbol{\beta}} = e^{\propto^* + \boldsymbol{X}_i{}'\boldsymbol{\beta}} \qquad [8]$$

where $\propto = e^{\propto^*}$. Note that when estimating a hazard ratio, the constant representing $h_0(t)$ disappears, and so [7] is a parametric PH model. This breakdown of the model to a PH model also occurs for an assumed Weibull distribution, but not Gompertz-Makeham, Gamma, log-Normal, or log-logistic.

Parametric models can also be fitted in the log(time) metric, that is, as an 'accelerated failure time' model which does not assume PH and instead specifies a constant for an increased or decreased relative effect between groups with time:

$$logT_j = \boldsymbol{X}_i'\boldsymbol{\beta} + \tau + \mu \qquad [9]$$

In order to choose an appropriate distribution for T (or the hazard or residuals), one can plot the hazard over time and choose a distribution that fits the restricted properties of the shape of the hazard. Relationships of the shape of the hazard function over time for assumed distributions of T are summarised in Table 5.5. Plotting the cumulative hazard function can also be helpful. For instance, if the cumulative hazard is constantly increasing, this indicates a constant hazard.

Figure 5.6 shows the form of the hazard $h(t)$ and $H(t)$ for the example of adolescent girls, for those admitted with accident-related injury. We could assume that this line was the form of the baseline hazard $h_0(t)$ (and baseline cumulative hazard $H_0(t)$) over time, and that there was no other unexplained variation of $h(t)$ among adolescent girls. One can see (more easily from the cumulative hazard plot than that of the hazard itself), that the hazard appears to monotonically increase, a property required for assuming an Exponential, Gamma, Gompertz-Makeham, or Weibull distribution (Table 5.5).

We can test whether the assumed distribution of T is a reasonable one by comparing resulting hazard ratios which those one would obtain from the semi-parametric PH model. We know that the semi-parametric PH model provides robust estimates of hazard ratios, and therefore an appropriate parametric model should result in similar hazard ratios with narrower confidence intervals. When a model was fitted to the example of adolescent girls assuming each of the above four distributions in turn (Table 5.6), it appeared that these assumed distributions were reasonable except for the Gamma distribution, which resulted in completely different coefficients when compared to the semi-parametric PH model. The 95% CIs were very similar between the semi-parametric PH, Exponential, Gompertz-Makeham and Weibull models.

Cleves summed up the choice between the semi-parametric PH and parametric models as follows:

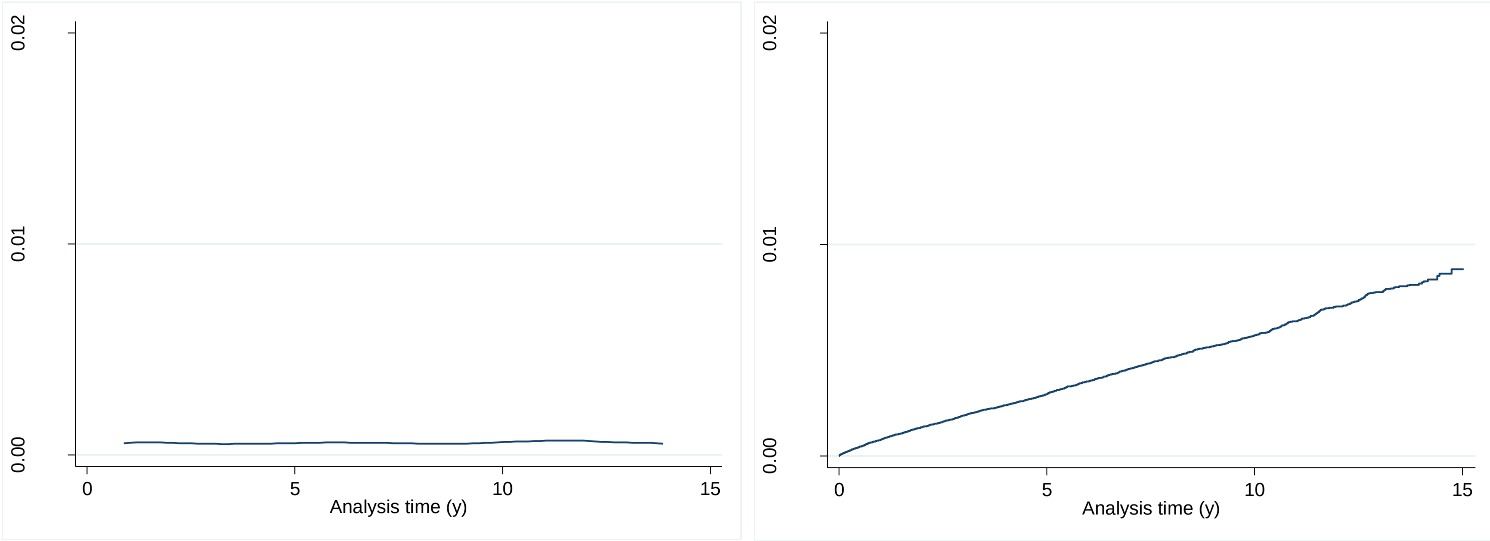
"If you are looking for parametrization of $h_0(t)$ that has considerable flexibility and has no restrictions on the shape of the hazard that you want to impose upon the model, we suggest you stay with Cox [semi-parametric proportional hazards] regression. That is what Cox regression does, and Cox regression does it well. Parametric estimation is only appropriate when you do have an idea of what the baseline hazard looks like and you want to impose the idea to 1) obtain the most efficient estimates of $\underline{\beta}$ as possible and 2) obtain an estimate of $h_0(t)$ subject to that constraint." (221)

In other words, parametric modelling can be useful when the exact values of the coefficients and predicted hazard (and therefore survival and failure) functions are of interest. However, when one wants to compare risks between groups, semi-parametric PH models are sufficient. Therefore for the purpose of analyses in Study II, I modelled times to death or emergency re-admission using semi-parametric PH models, unless there was evidence of a clear candidate distribution for T.

Table 5.5: Relationship of hazard function $h(t)$ with time, for different assumed distributions of event time T

Distribution of T	**Relationship of the hazard function $h(t)$ with time**
Exponential	Constant
Gamma	Constant, or monotonically increasing/decreasing
Gompertz-Makeham	Monotonically increasing/decreasing
Log-logistic	Initially increasing and then decreasing (or vice versa). Unimodal.
Log-Normal	Initially increasing and then decreasing (or vice versa). Unimodal.
Weibull	Monotonically increasing/decreasing

Sources: Princeton notes on 'Parametric Survival Models', German Rodriguez, last updated 2010 (236).



$h(t)$ = hazard function at time t; $H(t)$ = cumulative hazard function at time t

Figure 5.6: $h(t)$ and $H(t)$, against time since discharge from index admission for accident-related injury (example of adolescent girls*)

Table 5.6: Semi-parametric proportional hazards model vs. parametric models for different assumed distributions (example of adolescent girls)

Model	HR for adversity-related injury* (95% CI)	AIC
Semi-parametric PH	2.01 (1.81 to 2.24)	37,280
Exponential	2.02 (1.82 to 2.24)	22,353
Gamma	0.46 (0.41 to 0.52)	22,337
Gompertz-Makeham	2.01 (1.81 to 2.24)	22,354
Weibull	2.01 (1.80 to 2.23)	22,336

AIC = Akaike's Information Criterion, CI = Confidence Interval, HR = Hazard Ratio, PH = Proportional Hazards
*Risks of death for adolescent girls admitted as an emergency with adversity-related (vs. accident-related) injury

5.6 Methods for estimating cause-specific risks of death (Objective 5)

To estimate risks of death attributed to different causes (homicide, suicide drug/alcohol-related, accidental, and other causes) in Study III, I derived risks using cumulative incidence functions and estimated adjusted cause-specific hazards of death, using Fine & Gray sub-hazard models.

When estimating risks of death attributed to a specific cause, it was possible for the event to not only be censored by the end of data collection (in our case, March 31st 2012 or an individual turning 30 years old), but by deaths through different causes. For example, for risks of homicide, there were ‘competing risks’ of suicide, drug/alcohol-related deaths, accidental, and other causes. If homicides typically occurred soon after discharge from hospital, relative to the remaining causes (e.g., suicide), then the risk of homicide would have an impact on the risk of these remaining causes (e.g., patients who are at increased risks of homicide would appear to be at reduced risks from suicide). Therefore, risks of deaths attributed to different causes could be correlated. I used cumulative incidence functions and Fine & Gray models to account for these correlations. I also considered estimating cumulative failure functions semi-parametrically, using semi-parametric PH models and assuming competing events to be censored. However, this latter technique is complex, and less powerful than the former technique.

5.6.1 Cumulative incidence functions and Fine & Gray's sub-hazard models

Cumulative incidence functions

'Cumulative incidence functions' (CIFs; CIF_c for cause c), may be seen as the competing risks equivalent of cumulative failure functions (described in Section 5.4.1):

$$CIF_c(t) = P(T < t, failure\ from\ cause\ c) \qquad [10]$$

where $c = 1, \ldots . v$. CIFs may interpreted as the cumulative risks of an event of interest, given that none of the other competing risks has occurred (e.g., the cumulative risk of homicide for individuals who have not died from suicide) (221). CIFs are estimated as a function of risks of deaths by *all* competing causes:

$$CIF_c(t) = \int_0^t h_c(t) exp\left\{-\sum_{q=1}^{n_q} \int_0^x H_q(u)\right\} du \qquad [11]$$

where $q = 1, \ldots\ v_q$ are the remaining possible causes of death except for c. $h_c(t)$ represents the instantaneous risk of death by cause c (the cause-specific hazard) at time t:

$$h_c(t) = \lim_{\delta t \to 0} \left\{\frac{P(t \leq T < t+\delta, failure\ from\ cause\ c \mid T \geq t)}{\delta t}\right\} \qquad [12]$$

and $exp\left\{-\sum_{q=1}^{n_q} \int_0^x H_q(u)\right\} du$ is the probability of not dying through other causes (i.e., the survival function $S(t)$). The cause-specific hazard $h_c(t)$ is interpreted very similarly to the global hazard function: the instantaneous risk of an event through cause c given that the event has not occurred through any other cause (in the case of a non-renewable event such as death, this would be given that the event had not occurred at all).

It is important to note that the estimate of $CIF_c(t)$ in [11] is based on estimates for hazards of both the event of interest and all competing events (all other q causes). A non-parametric equation for the CIF_c based on the KM estimate of $S(t)$ is available in Cleves, 2010 (221).

Fine & Gray sub-hazard models

The CIF_c can also be indirectly estimated semi-parametrically through Fine & Gray subhazard models. These models result in the estimation of 'sub-hazard ratios' (SHRs). Fine & Gray's subhazard model takes a form similar to that of the semi-parametric PH model in [1]:

$$\bar{h}_c(t) = \bar{h}_{c,0}(t)e^{\boldsymbol{X'\beta}} \qquad [13]$$

The sub-hazard $\bar{h}_c(t)$ is interpreted in the same way as the general cause-specific hazard $h_c(t)$. The difference is in the estimation of $\bar{h}_c(t)$: in the case of $h_c(t)$, if a subject has an event through one of the q causes they do not contribute to $dN_i(t)$ in the PL in Equation [3]. However, for $\bar{h}_c(t)$ these subjects are not removed from the risk-set when estimating the hazard for cause c (237). They are included with their observations weighted according to when they are expected to be otherwise censored (i.e., in Equation [4], $Y_i(t)$ = 1 until the subject would be expected to be censored) (221).

The advantage of Fine & Gray's subhazard model is that SHRs are directly related to CIFs through the following equation:

$$CIF_c(t) = 1 - \exp \quad \{\int_0^t \bar{h}_c(u)\, du\}S \qquad [14]$$

Therefore, we can estimate adjusted CIFs by first estimating adjusted SHRs, and perform the transformation in [14]. Coefficients from [14] indicate the same increase or decrease on the CIF as on the SHR. In Study III, I used such SHRs (the outputs of Fine & Gray models) to report the adjusted effects of covariates on CIFs.

As an example, a Fine & Gray model was fitted to the data for adolescent girls, with accident-related death as the event of interest (cause 'c'), and adversity-related death (homicide, suicide or drug/alcohol-related) as the competing event (one of the 'q' causes) (Table 5.7). The resulting cause-specific CIFs were similar to those derived non-parametrically (point estimates were identical to two decimal places). This is likely due to the relatively low rates of death in this dataset, particularly when split into causes.

Table 5.7: Comparison of different methods for estimating cumulative risks of competing events (example of adolescent girls)

	HR for adversity-related injury* (95% CI)		AIC	10-year cumulative risk following adversity-related injury per 1,000 (95% CI)	
Event of interest: accident-related death**					
Non-parametric	.		.	1.2	(1.0 to 1.4)
Fine & Gray model	1.48	(1.15 to 1.90)	6,345	1.2	(1.0 to 1.3)
Semi-parametric PH model	1.48	(1.15 to 1.90)	6,345	1.2	(1.0 to 1.3)
Event of interest: other deaths***					
Non-parametric	.		.	2.2	(1.9 to 2.5)
Fine & Gray model	0.98	(0.84 to 1.15)	15,183	2.3	(2.1 to 2.5)
Semi-parametric PH model	0.98	(0.84 to 1.15)	15,181	2.3	(2.1 to 2.5)

AIC = Akaike's Information Criterion, CI = Confidence Interval, HR = Hazard Ratio, PH = Proportional Hazards
*Risks of death for adolescent girls admitted as an emergency with adversity-related (vs. accident-related) injury
**Where adversity-related deaths are considered competing events
***Where adversity-related and accident-related deaths are considered competing events

A requirement of Fine & Gray's model, as with the semi-parametric PH model, is the assumption of proportional sub-hazards on the event by cause c. Due to the weighting of observations, this assumption cannot easily be checked through plots of predicted against estimated survival as in Section 5.5.1, but can still be checked through introduction of a time-varying effect in the model and testing whether this effect is significantly different from 0.

5.6.2 Alternative methods

One could theoretically try to estimate CIFs adjusted for covariates by taking a non-parametric estimate of the baseline survivor function (e.g., KM estimate $\hat{S}_0(t)$), and using $\hat{S}_0(t)$ and coefficients estimated from the semi-parametric PH model, to derive the survivor function for the group/factor of interest (e.g., $S_{adversity}(t)$). The CIF could then be estimated through the relationship $F(t) = 1 - S(t)$. The semi-parametric PH model itself would be fitted as a regular semi-parametric PH model (as in Equation [1]; or parametrically if assuming a distribution for the baseline hazard function) but by treating times to competing events (through the q causes) as censored. However, this does result in subjects being dropped from the risk-set at particular time-points, who would otherwise remain in the case of fitting a Fine & Gray model.

Table 5.7 shows that when the CIF for accident-related death was estimated in the above way (semi-parametrically) for the example of adolescent girls (where adversity-related death was considered a competing event), the estimate did not differ greatly from those estimated non-parametrically. However, this CIF estimate is incredibly difficult to interpret since $S(t)$ should take the risks of events by all possible causes into account, but in this case has only incorporated risks through cause c (221).

5.7 Issue 1: Clustering of index emergency admissions for injury

5.7.1 The problem

To address Objectives 3 to 5, I estimated risks of outcomes following an index emergency admission for adversity-related (or accident-related) injury (Studies II and III). However, there could be multiple candidates for the index admission. That is, adolescents could have more than one emergency admission for injury between 10 and 19 years old (illustrated in Figure 5.1 in blue). Figure 5.7 shows the number of candidate index admissions, per adolescent, for the example of adolescent girls. The majority had only one candidate index (~88%) and around 10% had two, and the remaining 2% had three or more.

Times to outcomes from each of the multiple index admissions for the same adolescent were likely to be correlated with each other. For example, if we define the index admission to be the first emergency admission for adversity-related (or accident-related) injury, and the probability of death within ten years is high, we would expect the probability of death within ten years after a second emergency admission for adversity-related (or accident-related) injury to also be high. If all possible emergency admissions for injury per adolescent were treated as index admissions in analyses (without acknowledging this clustering), estimated risks could be biased. For time-to-event analyses specifically, not accounting for heterogeneity between times has been shown to over-estimate the 'true' time to an event and under-estimate standard errors of estimated coefficients in semi-parametric PH models (238).

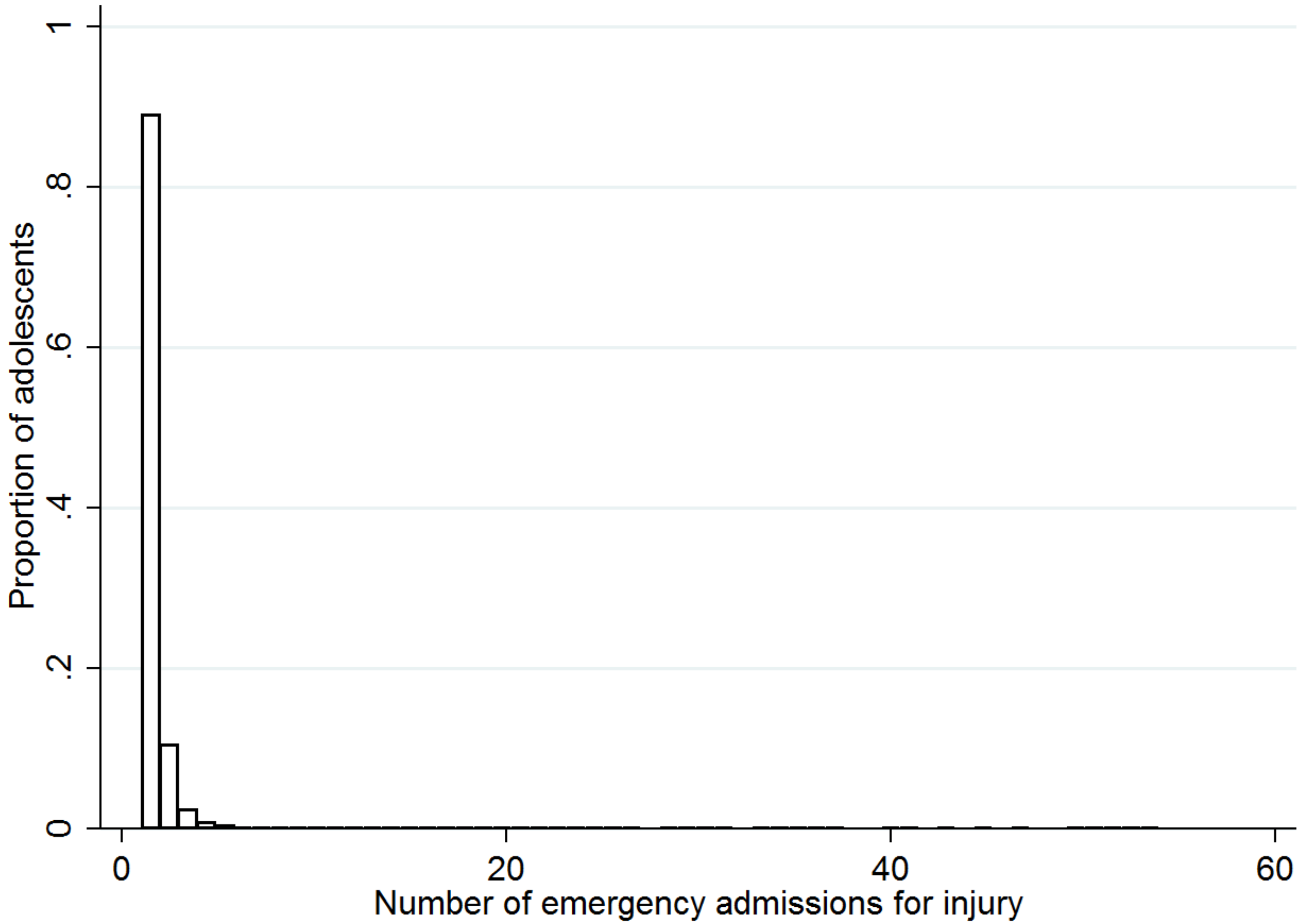


Figure 5.7: Distribution of numbers of emergency admissions for injury between 10 and 19 years old (example of adolescent girls)

5.7.2 Randomly selecting an index admission

To overcome the clustering of multiple emergency admissions for injury in Studies II and III, I randomly selected one emergency admission for injury (among the entire trajectory) to be the index, per adolescent.

Strengths and limitations

An advantage of randomly selecting an index admission is that this would represent what clinicians would see in practice, compared to other possible methods (e.g., taking the first such admission, which is described in the next section). From the results of Study I (Chapter 4), I expected 5 to 17% of adolescents to have more than one emergency admission for injury (depending on sex and types of injury). Therefore, 'extra' possible index admissions (those not randomly selected) were ignored for only a minority of adolescents in Studies II and III. In addition, cumulative risks could still be easily interpreted, compared to other possible methods.

One limitation of random selection of the index admission was that it was now possible that the prevalence of emergency admissions for adversity-related and accident-related injury would no longer be in proportion to that which is seen in hospital. For example, an adolescent who had two emergency admissions for accident-related injury and one for adversity-related injury would be more likely to have their admission for accident-related injury selected as the index admission (Figure 5.8). Therefore, if many adolescents in the extract of HES-ONS data had a high number of emergency admissions for accident-related injury compared with those for adversity-related injury, adolescents admitted with adversity-related injury could be under-represented. However, in Studies II and III, we did not seek to estimate the prevalence of admissions for adversity-related or accident-related injury (accomplished in Study I), but rather prognosis of outcomes following such admissions.

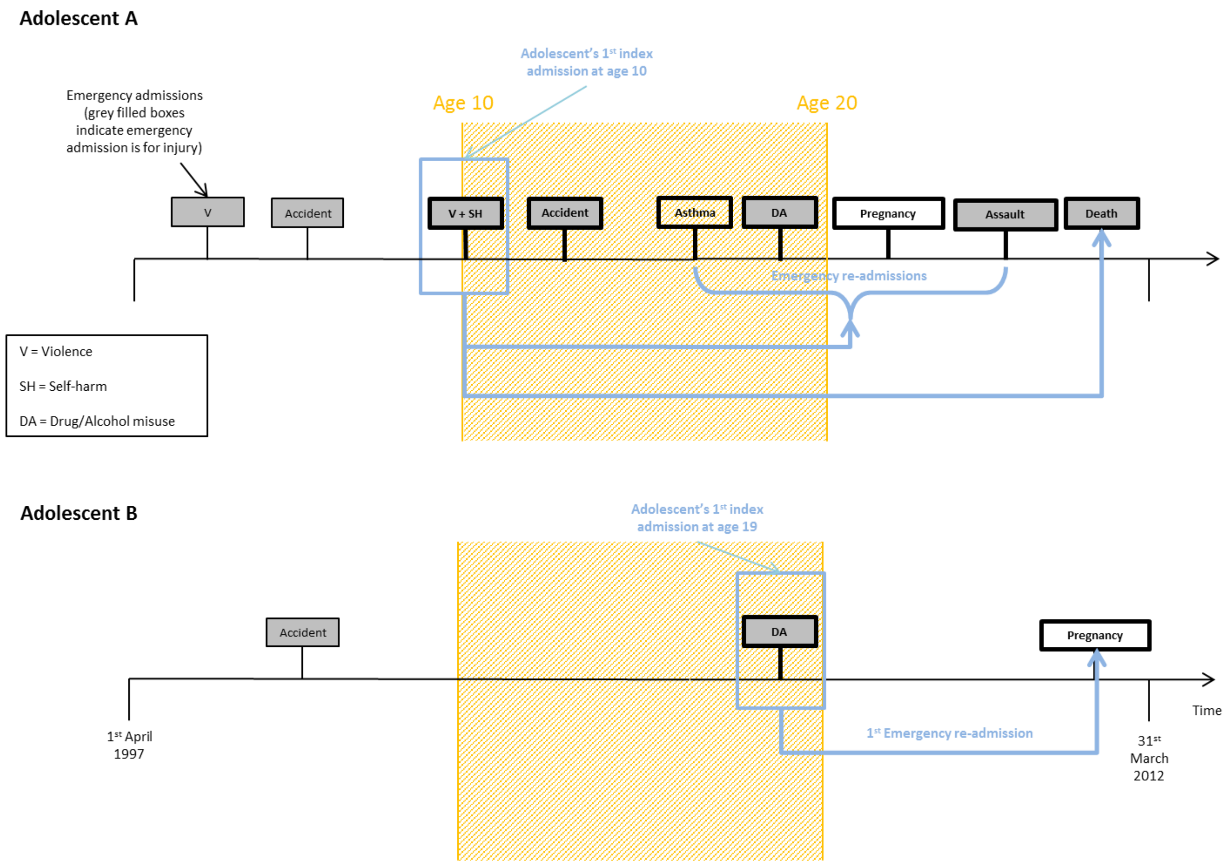
5.7.3 Alternative methods

Selecting the first or last emergency admission for injury

Instead of randomly selecting an index admission, I could have systematically chosen the first or last emergency admission for injury in the adolescents' trajectories of such admissions. However, this method could bias coefficients in either direction, which in turn means that results can be difficult to interpret.

Figure 5.8 demonstrates the potential bias using two adolescents' possible trajectories of emergency admissions for injury. Adolescent A had his first emergency admission for injury at 10 years old, and Adolescent B had his at 19 years old. We would expect these adolescents to have very different trajectories of emergency admissions. For example, Adolescent B may have had fewer health problems during adolescence than Adolescent A (and therefore perhaps had a better prognosis). He could also have better concealed his health problems (and therefore perhaps had a worse prognosis). The latter scenario is common in cases such as alcohol disorders, that are often not diagnosed until young adulthood (239).

Table 5.8 shows the results when fitting a semi-parametric PH model to data for the example of adolescent girls, first assuming the first emergency admission for injury to be the index (the event being death), and then when assigning the index to be a randomly selected emergency admission for injury. In this case, the resulting estimated HRs for adversity-related (versus accident-related) injury were similar (both were ~2.00).



Time not to scale.
*In interest of data security, this is not a true trajectory for an adolescent in the HES-ONS dataset, but is based on true trajectories.

Figure 5.8: Hypothetical trajectory of admissions*, to illustrate different possible trajectories according to age at first emergency admission for injury

Table 5.8: Comparison of different methods for selecting an index admission (example of adolescent girls)

Selection of index admission	HR for adversity-related injury* (95% CI)	Variance of frailty term, θ (p-value for H_0: $\theta = 0$)	AIC
All girls			
First emergency admission for injury	2.01 (1.81 to 2.24)	.	37,280
Randomly selected	1.99 (1.78 to 2.21)	.	36,016
All emergency admissions for injury (Gamma**)	Could not be estimated	Could not be estimated	.
All emergency admissions for injury (Inv-Gauss***)	Could not be estimated	Could not be estimated	.
Girls with ≥ 6 emergency admissions for injury at 10-19 years old			
First emergency admission for injury	4.79 (1.17 to 19.64)	.	786
Randomly selected	4.25 (0.59 to 30.74)	.	739
All emergency admissions for injury (Gamma**)	3.19 (1.50 to 6.78)	231.06 (<0.001)	5,550
All emergency admissions for injury (Inv-Gauss***)	Could not be estimated	Could not be estimated	.

AIC = Akaike's Information Criterion, CI = Confidence Interval, HR = Hazard Ratio
*Risks of death for adolescent girls admitted as an emergency with adversity-related (vs. accident-related) injury
**Gamma distributed shared frailty term in model
***Inverse-Gaussian distributed shared frailty term in model

Shared frailty models

One can analyse data on clustered times whilst accounting for this clustering, through 'shared frailty' models (240, 241). These models are simply time-to-event models that include a random intercept per subject (the 'shared frailty' term). For example, a shared frailty semi-parametric PH model takes the form:

$$h_i(t) = h_0(t)e^{\boldsymbol{X}_i{}'\boldsymbol{\beta}+\omega_i} \qquad [15]$$

where ω_i, is some constant specific to subject i. The shared frailty term is e^{ω_i} and increases the hazard $h(t)$ for subject i multiplicatively. The higher the value of ω_i, the higher the hazard for that particular adolescent. Since ω_i should account for some within-subject variance that is not accounted for by other covariates, its inclusion should improve model fit. An assumed distribution for ω_i must be specified. This distribution is commonly assumed to be Gamma or inverse-Gaussian (227).

The shared frailty model is usually estimated by maximising a penalised version of the partial likelihood (PPL):

$$PPL = \ l(\boldsymbol{\beta}, \omega) - g(\omega; \boldsymbol{\alpha}) \qquad [16]$$

where $l(\beta, z)$ is the log of the partial likelihood (the same likelihood that is maximised in regular semi-parametric PH model estimation). $g(\omega; \boldsymbol{\alpha})$ is a constraint which assigns penalties to values of ω, and $\boldsymbol{\alpha}$ is a vector of 'tuning parameters' from the distribution of ω. That is, the likelihood is fitted to a range of values from ω ($\boldsymbol{\alpha}$) and the maximum of the resulting PPLs is taken forward ('tuning').

One considerable limitation of the shared frailty model is that more degrees of freedom are needed to include and estimate the distribution of the frailty term, compared to the regular time-to-event model that does not include the term. This is a clear limitation when we consider the data used in Studies II and III. In the (similar) data for the example of adolescent girls, there is a large number of clusters with few data points (i.e., $i = 1,2, \ldots 350236, 350237$). Within each of these 350,237 clusters, nearly all of these clusters had only one or two data-points (98%), which contribute to the PPL. Therefore as shown in Table 5.8, when a shared frailty model is fitted to these data (assuming either a Gamma or inverse-Gaussian distributed frailty term, in turn), the model cannot be estimated. It is possible to fit such a model to a subset of these adolescents who had at least six or more emergency admissions for injury (n=18,653; Table 5.8), where the number of clusters is much smaller and the number of data-points per cluster bigger. As one might expect, among this sub-group of adolescents who were admitted with injury the most often, the HR for death in this subset (4.25) is greater than that for the entire group (randomly selected index, whole sample: 1.99).

In Studies II and III, the dataset was larger than that for adolescent girls, but the distribution of numbers of candidate index admissions was likely to be similar. Therefore, it was very likely that there would not be enough degrees of freedom with which to fit a frailty model. Even if it was possible to fit such a model, the loss of precision around the estimated HR for adversity-related (versus accident-related) injury compared to that from a model using a randomly selected index admission was unlikely to be compensated by the 'extra' index admissions included (on a minority of adolescents).

5.8 Issue 2: Recurrent events

5.8.1 The problem

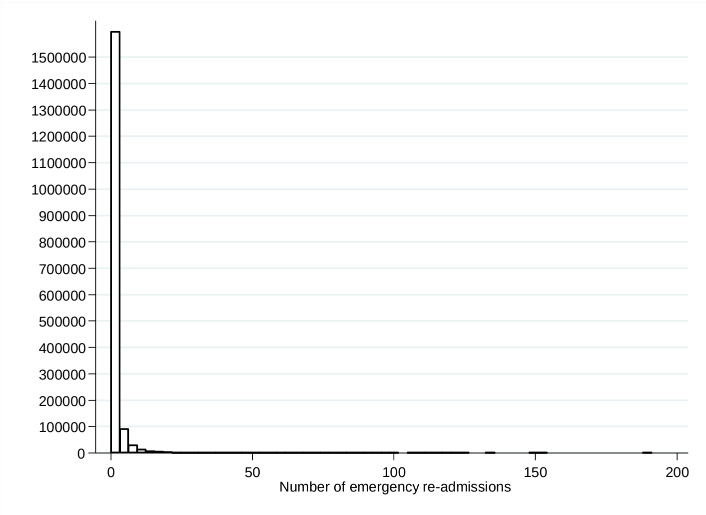
One of the events within Study II, an emergency re-admission, was a 'recurrent event'. That is, an event that could occur multiple times during follow-up (illustrated in Figure 5.1 in red). Recurrent emergency re-admissions were likely to hold valuable information about the burden of adversity-related injury. Firstly, the more emergency re-admissions, the greater the use of healthcare and the greater the burden on the individual adolescent. Indeed, Lilley *et al* found that among patients (of all ages) presenting to a hospital with self-inflicted injury, 17% of their first presentations were followed by a repeat presentation in the next 18 months, but 33% of all presentations were followed by another presentation in one year (184). Ignoring 'extra' presentations for self-inflicted injury following the first repeat presentation almost halved the estimated burden on hospitals from patients in this study.

Secondly, multiple emergency re-admissions could identify a sub-group of adolescents with a greater vulnerability and severity of adversity, compared to those re-admitted only once. For example, even if adolescents with adversity-related injury were just as likely to be re-admitted as an emergency as those with accident-related injury, it could still be that a larger proportion of those with adversity-related injury are likely to be admitted multiple times over the same time-period.

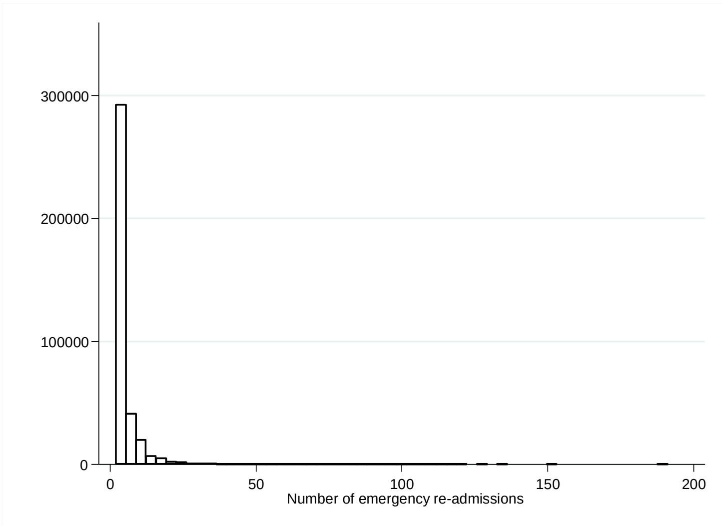
In Study II, risks of not only the first emergency re-admission following an index emergency admission for injury were of interest, risks of subsequent emergency re-admissions were too. For the example of adolescent girls, the majority did not have an emergency re-admission over the next 14 years (the maximum follow-up) (Figure 5.9, a). However, among those that did have an emergency re-admission, a substantial proportion had two, three, four, or five (Figure 5.9, b). Therefore, in Study II risks of second to fifth recurrent re-admissions were reported alongside risks of a first re-admission, where possible.

Recurrent events on the same individual could not be analysed as though from separate individuals, as there was likely to be a dependence between events for the same individual, particularly when covariates affecting these events were not included in analyses (227). Ignoring clustering of events has been shown to produce substantially biased parameter estimates (242). For the final analyses in Study II, I employed Wei, Lin & Weissfeld (WLW) and Prentice, Williams & Peterson's (PWP; with 'gap-times') approaches to include recurrent emergency re-admissions and account for the correlations between these re-admissions. I also considered other 'variance-corrected' models, as well as shared frailty and mean/rate models. However, these latter methods required assumptions of event rates that were unlikely to be well met in Study II.

a)



b)



*Emergency re-admissions in the ten years following a first emergency admission for adversity-related or accident-related injury

Figure 5.9: Numbers of emergency re-admissions (example of adolescent girls*), a) for all adolescents, b) for adolescents who had one or more emergency re-admissions

5.8.2 Wei, Lin & Weissfeld (WLW) and Prentice, Williams & Peterson (PWP) gap-time approaches to modelling recurrent events

The WLW approach

The WLW approach can be applied to any time-to-event model. Recurrent events $k\ (k = 1, ...\ m)$ are included in the model, which is stratified by the event order (1st, 2nd,…mth event). For example, if employing a WLW semi-parametric PH model, the model is fitted as follows, where k represents each stratum:

$$h_{ik}(t) = h_{0k}(t)e^{\boldsymbol{X}_i{}'\boldsymbol{\beta}_k} \qquad [17]$$

The treatment effect $\boldsymbol{\beta}$ is estimated by maximisation of the partial likelihood:

$$PL(\boldsymbol{\beta}) = \prod_{j=1}^{J} \frac{h(t_{(j)})}{\sum_{k\,\epsilon\,R(t_{(j)})} h(t_k)} \qquad [18]$$

where ordered event times are $t_{(1)<}\,t_{(2)<}\,\cdots\ t_{(\tau)}$ and $R(t_{(j)})$ defines the risk-set of individuals at time-point $t_{(j)}$. In the case of the WLW method, this risk-set includes all subjects. The number of strata is equivalent to the maximum number of events that an individual subject has had and all subjects contribute to each stratum.

$\boldsymbol{\beta}_k$ is the treatment effect for the kth event. An overall $\boldsymbol{\beta}$, for the cumulative effect across all strata may be estimated by either 1) constructing an overall $\widehat{\boldsymbol{\beta}}$ as the weighted average of $\widehat{\boldsymbol{\beta}}_k$'s that achieves the minimum possible variance (243), or 2) fitting a model with the constraint that all $\boldsymbol{\beta}_k$'s be equal (227). Estimating an overall $\boldsymbol{\beta}$ can prove useful when there are so many strata, that the corresponding number of estimates of $\boldsymbol{\beta}_k$ cannot be meaningfully interpreted. However, such a $\boldsymbol{\beta}$ only validly represents the general effect across strata, when their corresponding effects are not too dissimilar.

The WLW approach can be used to compare average group responses whilst correcting the covariance matrix of the $\widehat{\boldsymbol{\beta}}$ estimates for clustering (using the sandwich estimator) (244). That is, it is a 'variance-corrected' model, with the advantage that it does not require explicit estimation of the correlations between multiple times within individuals. Another advantage of the WLW approach is that the same subjects at baseline, and their covariates, remain in each stratum analogous to an 'intention-to-treat' analysis. In the case of RCTs for example, the randomisation is preserved. However, this advantage is offset by a bias in estimated coefficients with increasing strata, where coefficients are over-estimated (243, 245, 246). Though a variance correction could go some of the way to reducing the over-inflation of standard errors, they could still be often over-estimated.

Table 5.9 shows the results when fitting a model using the WLW approach in the example of adolescent girls, including adversity-related (versus accident-related) injury as an independent covariate, and the first five emergency re-admissions as events. The coefficient for adversity-related injury increases with increasing order of event. The same adolescents that are at high risk of a first emergency re-admission in stratum 1 (those with adversity-related injury) are the only subjects that can have a second re-admission in stratum 2 (227). Risks estimated in each stratum are not 'memoryless': whatever occurs in stratum 1 has a bearing on what occurs in stratum 2, and later strata.

Table 5.9: Comparison of different models for recurrent events (example of adolescent girls)

	HR for adversity-related injury* (95% CI)			
Event	**WLW**	**PWP Gap-time**	**PWP Elapsed Time**	**PWP Counting Process**
1st	1.85 (1.83 to 1.87)	1.85 (1.83 to 1.87)	1.85 (1.83 to 1.87)	1.85 (1.83 to 1.87)
2nd	2.25 (2.22 to 2.28)	1.45 (1.43 to 1.47)	1.64 (1.62 to 1.67)	1.42 (1.40 to 1.44)
3rd	2.47 (2.42 to 2.52)	1.20 (1.18 to 1.23)	1.45 (1.43 to 1.48)	1.08 (1.06 to 1.10)
4th	2.59 (2.53 to 2.66)	1.10 (1.08 to 1.13)	1.34 (1.31 to 1.38)	0.95 (0.93 to 0.97)
5th	2.68 (2.61 to 2.76)	1.07 (1.03 to 1.10)	1.27 (1.23 to 1.31)	0.91 (0.88 to 0.93)
Overall**	2.14 (2.11 to 2.16)	1.53 (1.51 to 1.54)	1.66 (1.64 to 1.67)	1.47 (1.46 to 1.49)
AIC (for overall)	7,594,377	7,068,022	7,073,475	6,679,750

AIC = Akaike's Information Criterion, CI = Confidence Interval, HR = Hazard ratio, PWP = Prentice, Williams & Peterson, WLW = Wei, Lin & Weissfeld
*Emergency re-admissions in the ten years following a first emergency admission for adversity-related (vs. accident-related) injury
** HRs were estimated by constraining model such that all $\boldsymbol{\beta}_k$s were equal.

PWP Gap-time models

The PWP approach, like WLW, takes any time-to-event model and stratifies it by the k events, the coefficients are estimated using the PL, and the variance of these coefficients are corrected. However in addition, the PWP model is conditional: a subject may only appear in strata for the k^{th} event if they have experienced the $(k-1)^{\text{th}}$ event. That is, the risk set is re-set. Therefore, $\boldsymbol{\beta}_k$ can be interpreted as the treatment effect after having had the $1, \ldots (m-1)$ other events.

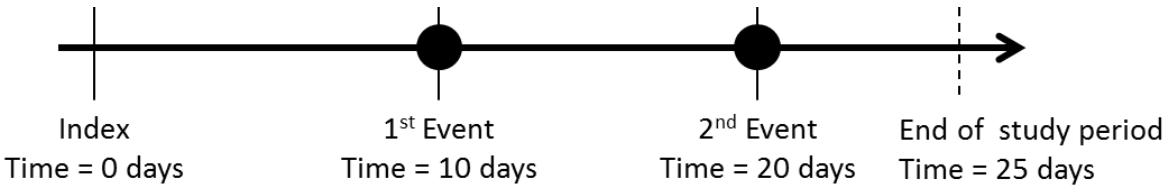
The PWP approach does not suffer the same bias in its estimation of coefficients as WLW methods. Only a subset of subjects appear in stratum 2, who all had a first event, and so only remaining information should affect whether they have a second event. However, this advantage is offset by the fact that the distribution of covariates is not the same within each strata (227).

Table 5.9 shows that when fitting a PWP gap-time (PWP-GT) model for the example of adolescent girls, the coefficients decrease with increasing strata. As those with adversity-related injury were more likely to have a first emergency re-admission than those with accident-related injury, these adolescents were more likely to 'go through' to stratum 2. By stratum 4 or 5, we are no longer comparing adversity-related with accident-related injury as it naturally occurs within a hospital setting.

Time entry

Though there is only one way of entering times-to-events for the WLW approach, there are three ways that time-to-events can be entered for the PWP approach (Prentice *et al* discussed only two in their first report of this method (247); Kelly *et al* have since pointed out that a third is possible (245)).

These three times are illustrated in Figure 5.10. Time can be entered as either 1) ‘Gap-time’ (GT): time since the latest event and the clock re-set at zero after each event, 2) ‘Elapsed time’ (ET): time since the index, for all events, or 3) ‘Counting process’ (CP): time since the latest event but without the clock re-set at zero after each event (248). GT entry models have been shown to produce less biased estimates compared with corresponding CP or ET models (245, 248). Table 5.9 shows that in the example for adolescent girls, the estimated risk when using the PWP-GT approach, lies somewhere between that for the PWP-ET and PWP-CP approaches. For Study II, I decided to fit PWP models with gap-time entry.



	Interval	Strata (Event Number)
PWP elapsed time	(0, 10]	1
	(0, 20]	2
	(0, 25)	3
PWP gap time	(0, 10]	1
	(0, 10]	2
	(0, 5)	3
PWP counting process	(0, 10]	1
	(10, 20]	2
	(20, 25]	3

Figure 5.10: Data entry for different PWP approaches to recurrent event modelling

Why both WLW and PWP models?

For Study II, I employed both WLW and PWP models so that I could get an understanding of the relative change in risk after discharge (baseline), of a subsequent event according to adversity-related (versus accident) related injury. The PWP model has been shown to produce the least biased estimates among these seven (245, 248). In fact, it has been shown to often under-estimate coefficients. However, the differences in risk are more validly interpreted from WLW models. Therefore, I reported results from both approaches alongside each other and assumed that that the ‘true’ effect was somewhere between the two.

5.7.4 Alternative methods

Table 5.10 shows seven possible variance-corrected models (including WLW and PWP) for analysing recurrent events. These methods only differ in how they define 1) the baseline hazard, 2) the risk-set of individuals over time, 3) risk (or time) –intervals and 4) how within-subject correlations are handled (245). Fixing three of these four elements automatically decides the choice of the fourth and so I describe the first three in Table 5.10. A description of baseline hazards, risk-sets, risk-intervals and within-subject correlation, and how they relate to these seven models is available from Kelly & Lim, 2000 (245).

In Study II, I did not employ an unrestricted GT, a Lin, Wei & Amato, or an Andersen-Gil model, as all three of these models assume a common baseline hazard between all events (and unrestricted risk-sets) whatever their order. In Study II, the same baseline hazard for a second emergency re-admission as for a first was unlikely (and for a third, and so forth). In the example of adolescent girls, they were at greater risk of first emergency re-admissions than second or third.

One can also model the recurrent event times in shared frailty models (discussed earlier in 5.6). However, such models do not take into account the ordering of the events which is likely to be important in the case of emergency re-admissions following adversity-related injury. We cannot assume that adolescents in Study II were at just as much risk of a second re-admission as a first.

Finally, another option is to use mean and rate functions to model the recurrent events. That is, to assume an underlying Poisson process and model the effect of covariates on the mean and rates of this process (249). However, in Study II there were unlikely to be enough recurrent events per adolescent (or variation in numbers of events) for such a model to be fitted (Figure 5.9), and even then, for results to be meaningful.

Table 5.10: Different marginal methods for analysing recurrent events, by model features.

	Baseline hazard and risk-set		
Risk interval	**Common hazard and unrestricted**	**Event-specific hazard and semi-restricted**	**Event-specific hazard and restricted**
Gap time	Unrestricted Gap Time (245)	Not possible	PWP Gap Time (247)
Total time	Lee, Wei & Amato (250)	WLW (251)	PWP Elapsed Time (245)
Counting process	Andersen-Gil (252)	Possible but makes no sense*	PWP Counting Process (247)

Table adapted from PJ Kelly & LLY Lim, Stat Med 2000 (245)
PWP = Prentice, Williams & Peterson; WLW = Wei, Lin & Weissfeld
*Counting process intervals imply that a subject is never at risk for a k^{th} event at the same time as the $(k-1)^{th}$ event or the $(k+1)^{th}$ event (see Figure 5.10). However, a semi-restricted risk-set allows a subject who has had only k-1 events to be at risk for the k^{th} event.

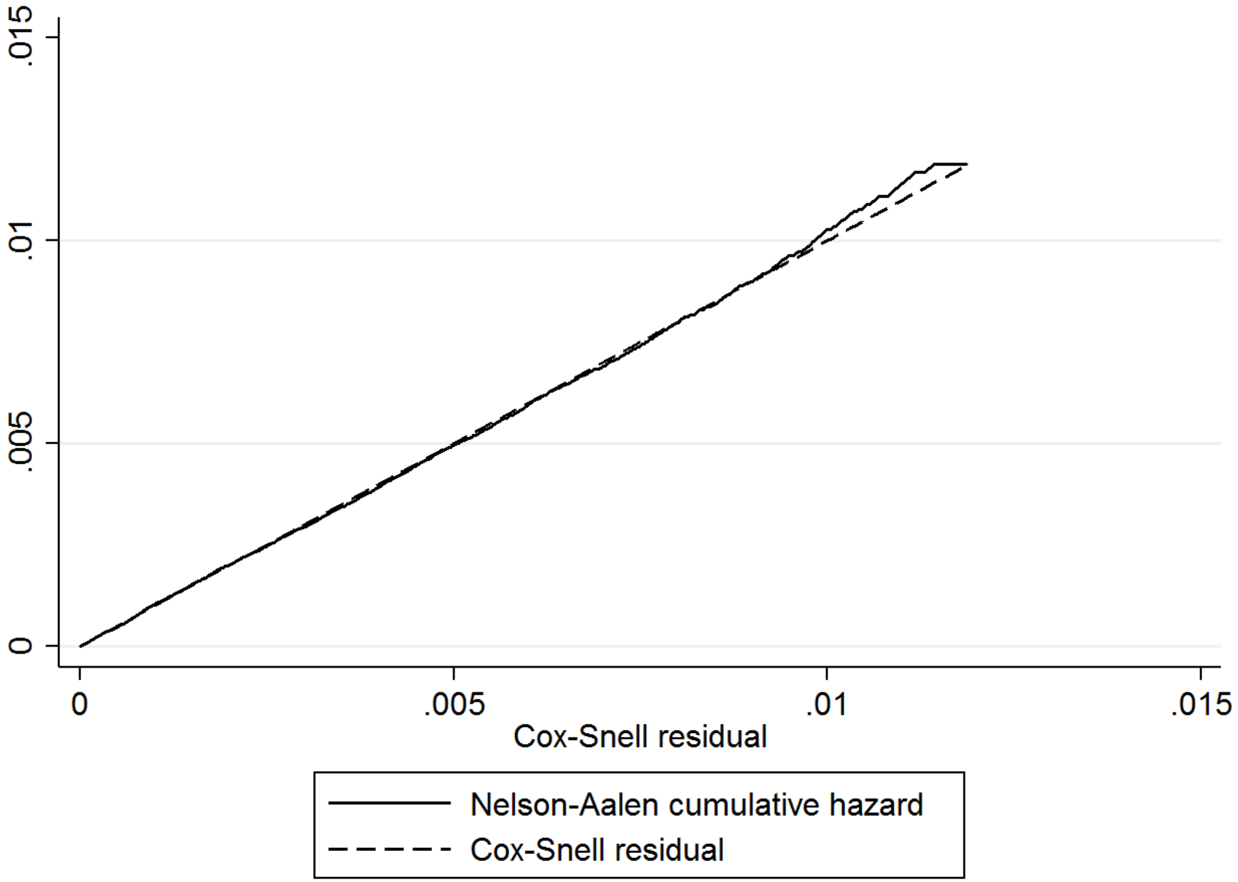
5.9 Goodness-of-fit

'Goodness-of-fit' is the amount of discrepancy between a model's fit and the observed data. Model statistics on goodness-of-fit can be used to determine between several options of statistical methods. For example, such tests may be used to compare the fit of a semi-parametric PH model and a parametric model to the same set of data. Furthermore, goodness-of-fit measures are important for assessing the specification of covariates and their functional forms in the selected model. For example, these measures could be used in Study II for deciding on whether to include a term for ethnicity or interaction terms in final analyses.

In Study II, I used plots of Nelson-Aalen estimates of the cumulative hazard function against Cox-Snell residuals to assess overall model goodness-of-fit (221). Cox-Snell residuals for an estimated model have the form:

$$CSr_j = \hat{H}(t_j|\boldsymbol{X}) = \hat{H}_0(t_j)e^{x_j\hat{\boldsymbol{\beta}}} \qquad [19]$$

It has been shown that $H(t|\boldsymbol{X}) \sim Exp(\ )$ and $h(t) = 1, \forall\, t$ (253). Therefore, a plot of the cumulative hazard of $H(t)$ against CSr_j should produce a 45 degree straight line. Figure 5.11 shows the Cox-Snell plot for the example of adolescent girls, fitting a semi-parametric PH model where the outcome is emergency re-admission, and the independent variable is adversity-related (versus accident-related) injury. The smoothed plot of Cox-Snell residuals (solid) line agrees well with the 45 degree (dashed) line.



Index admission defined as first emergency admission for injury; event is death, independent variable adversity-related (vs. accident-related) injury at index. Plot is for semi-parametric PH model.

Figure 5.11: Cox-Snell plot (example of adolescent girls)

One limitation of the Cox-Snell plot, as for other graphical tests (see Section 5.5.2), is that its interpretation is subjective. In the example above (Figure 5.11), there is almost a perfect fit and so interpretation is not difficult. A more formal way of testing goodness-of-fit is via the 'link test':

$$\log\left(\frac{h_A(t)}{h_B(t)}\right) = \rho_1(\widehat{\boldsymbol{\beta}}'\boldsymbol{X}) + \rho_2(\widehat{\boldsymbol{\beta}}'\boldsymbol{X})^2 \qquad [20]$$

A test for the null hypothesis $\rho_2 = 0$ would reveal whether $(\widehat{\boldsymbol{\beta}}'\boldsymbol{X})^2$ is significant or not, and therefore whether there are covariates in the linear predictor $\widehat{\boldsymbol{\beta}}'\boldsymbol{X}$ that should be included in the model in a higher-dimensional form. That is, whether or not there has been a poor model specification.

Using the example for adolescent girls, I fitted a semi-parametric PH model, including adversity-related (versus accident-related) injury and age group as covariates; ρ_1 was estimated to be statistically significantly different from 0 ($\rho_1 = 0.97$; p-value < 0.0001) indicating that $\widehat{\boldsymbol{\beta}}'\boldsymbol{X}$ captured some information about the outcome, whereas ρ_2 was not ($\rho_2 = 0.03$; p-value = 0.85), which indicated that the model had been adequately specified.

5.10 Discussion

In this chapter I have considered several established statistical methods for time-to-event data, to address Objectives 3 to 5 and account for multi-level properties of the HES-ONS data extract.

To illustrate how these methods may be applied, and results interpreted, I employed them in a subset of the HES-ONS data. I discussed how estimates from these different methods could vary for the same research question. In fact, within this subset of the data, the choice of methods showed a relatively negligible impact on the principal outputs. For example, the increase in risks of death and emergency re-admissions for adolescents with adversity-related (versus accident-related) injury (Objective 4; the increase was approximately double, regardless of the choice of method). The majority of selected methods were established in both the statistical and clinical research literature (e.g., cumulative failure functions, semi-parametric PH models, shared frailty models). Therefore, the majority of results in Studies II and III may be relatively easily interpreted without much background explanation to the methods used.

The HES-ONS data extract and designs of Studies II and III did pose additional methodological challenges, for example, recurrent events. Therefore, more novel methods were required to deal with these issues, for example the WLW and PWP-GT methods (254, 255). Though literature on these methods was scarce, the application of these methods in the data for adolescent girls was straightforward with just as easy to interpret results. Further reporting of WLW and PWP methods within the clinical literature could motivate their use and discourage analysing time-to-event data only for the first event (and thus waste of information).

Shared frailty models could not be run on the large HES-ONS dataset for adolescent girls where few had more than one index. Simulation studies indicating adequate data structures, with which to fit shared frailty models, would be useful for understanding when they could be employed in big datasets.

In conclusion, the methods applied in Studies II and III have been considered and selected amongst a larger set of established statistical methods for the same research questions. The review of these methods in the current chapter has highlighted a need for more methodological studies into ways of handling recurrent events and shared frailty models within large datasets, as well as work to encourage more mainstream use of these methods in the literature. Though results of the above two studies may have been marginally influenced by choice of statistical method, some prior exploration in an example dataset indicates that this influence would not substantially alter the overall conclusions.

Chapter 6 Study II, Risks of death and emergency re-admissions following adversity-related injury (Objectives 3 and 4)

6.1 Chapter summary

The current chapter describes the methods, results and interpretation for addressing Objectives 3 and 4 of this thesis. That is, to estimate risks of death and emergency re-admission following an emergency admission to hospital for adversity-related injury during adolescence, and to compare these risks to those following accident-related injury.

Using HES-ONS data for 1997-2012, I derived a cohort of adolescents who were admitted as an emergency with injury between 10 and 19 years old. I first estimated ten year risks of death and emergency re-admission after discharge, using Kaplan-Meier functions, and compared risks between adversity-related and accident-related injury. I then compared these risks whilst adjusting for age, ethnicity, deprivation, and chronic condition status, using semi-parametric proportional hazards (PH) regression. I used Wei, Lin & Weissfeld and Prentice, Williams & Peterson approaches, to estimate relative risks of a 2nd, 3rd, 4th, and 5th emergency re-admission. All analyses were stratified by sex.

Among 333,009 adolescents admitted with adversity-related injury, 1 in 137 girls and 1 in 64 boys died in the ten years after discharge, compared to 1 in 270 and 1 in 137 of the 629,818 adolescents admitted with accident-related injury; 54.2% of girls and 40.5% of boys with adversity-related injury had an emergency re-admission (compared to 36.1% and 30.2% respectively, among those with accident-related injury). After adjustment for age, girls and boys with adversity-related injury were estimated to be at 41% to 113% times higher risks of death and emergency re-admission (and of a 2nd, 3rd, 4th or 5th) than those with accident-related injury (varying by sex and outcome; further adjustment for other factors did not substantially alter hazard ratios [HRs] in semi-parametric PH regression results). Risks were increased following all types of adversity-related injury, and were particularly increased following self-inflicted or drug/alcohol-related injury (e.g., age-adjusted HR of death for boys with self-inflicted and drug/alcohol-related injury [vs. accident-related injury]: 3.41, 95% confidence interval: 3.11 to 3.74).

This chapter ends with a discussion of the main findings, strengths and limitations unique to this study, and implications of these results for policy and practice. National clinical guidelines for managing adolescents admitted with violent or drug/alcohol-related injury should be developed to reflect the fact that risks of future harm in these adolescents are similar to those admitted with self-inflicted injury. Interventions that can be delivered close to the time of discharge, and that are effective for reducing risks of future harm, are needed. Such interventions need to accommodate high-risk groups, such as older adolescents and those with chronic conditions.

6.2 Introduction

In Chapter 1, it was shown that there is a lack of studies that have 1) examined risks of harm following all three types of adversity-related injury within the same group of adolescents, 2) estimated risks of all-cause outcomes (e.g., re-injury, re-admissions, deaths), other than repeat injury related to the same type of adversity (e.g., repeat violent injury following an initial violent injury), or 3) compared risks of future harm to those in other adolescents (e.g., those presenting with other types of injury). Therefore, Objectives 3 and 4 of this thesis were to:

4. *Estimate the absolute risks of death and emergency re-admission in the ten years after discharge from an emergency admission for adversity-related injury during adolescence.*
5. *Compare risks of death and emergency re-admission following adversity-related injury with those following accident-related injury.*

This Chapter describes analyses and results of Study II, which addressed these objectives. The main results from this chapter were published in *Plos Medicine* (256). The full article is available in Appendix D.2.

6.3 Methods

6.3.3 Study cohort and admissions

Using HES-ONS data, I identified adolescents (aged 10-19 years inclusive) who had one or more emergency (acute, unplanned) admission(s) for injury (Figure 6.1). Admissions and emergency admissions for injury were defined as described in Section 3.3.5. Most adolescents (89%) had only one emergency admission for injury during the study period, which was defined as the index admission. For adolescents who had two or more emergency admissions for injury, I randomly selected one as the index admission (discussed further in Section 5.7.2). Adolescents who died at the index admission (n=1,877) were excluded from analyses.

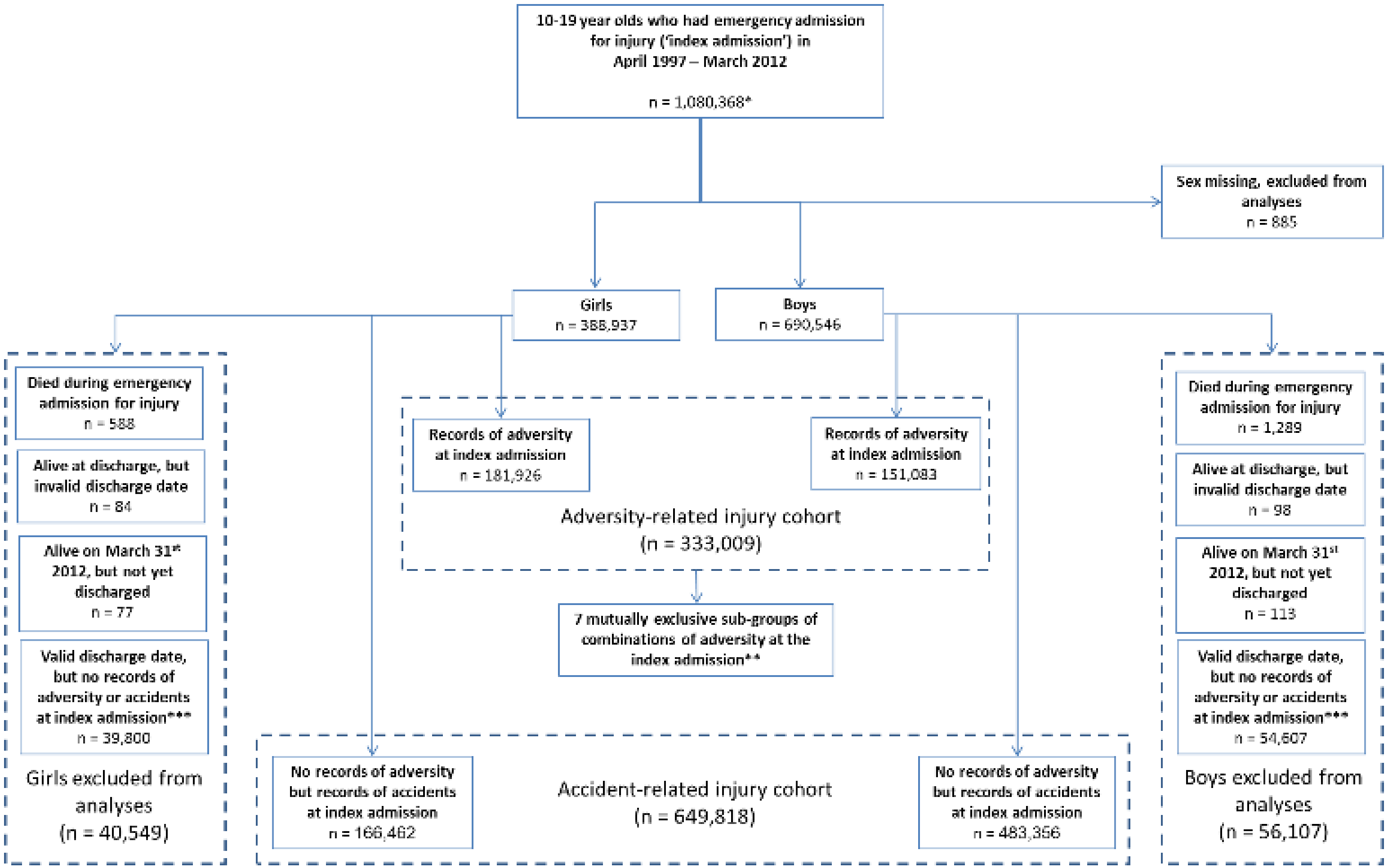
HES year	97/98	98/99	99/00	00/01	01/02	02/03	03/04	04/05	05/06	06/07	07/08	08/09	09/10	10/11	11/12
					0	1	2	3	4	5	6	7	8	9	10
				0	1	2	3	4	5	6	7	8	9	10	11
			0	1	2	3	4	5	6	7	8	9	10	11	12
		0	1	2	3	4	5	6	7	8	9	10	11	12	13
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Age	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
	17	18	19	20	21	22	23	24	25	26	27	28	29	30	
	18	19	20	21	22	23	24	25	26	27	28	29	30		
	19	20	21	22	23	24	25	26	27	28	29	30			

*Striped area represent at ages at w hich adolescents and their admissions w ere studied. Solid grey area represents w hen an adolescent could have an ‘index’ admission (from w hich to estimate risks of death or emergency re-admission).

Figure 6.1: Cohort of individuals who had at least one emergency admission for injury at 10-19 years old and in April 1997-March 2012*

6.3.4 Adolescent groups

I used ICD-10 codes recorded at the index admission to define two distinct groups of adolescents who were alive at discharge (Figure 6.2). I defined one group of adolescents whose index admission was for adversity-related injury (i.e. codes indicating any injury coupled with violence, intentional self-harm or drug/alcohol use). The comparison cohort comprised adolescents whose index admission record had no codes indicating adversity-related injury but codes indicating accident-related injury. All of these codes are described in Appendix C.2.



*was not possible to impute any missing values at 0-30 years old

Figure 6.2: Formation of adversity-related injury and accident-related injury cohorts among 10-19 year olds, for Study II

6.3.5 Outcomes

The outcomes of interest were death and emergency re-admission at least one day after discharge from the index admission and within the next ten years. I identified incidence and dates of deaths through linked ONS mortality data, and emergency re-admissions and their dates from HES (multiple admissions on the same adolescent were linked within HES; described in Section 3.3.2).

6.3.6 Confounding and independent variables

I included age-group (10-14, 15-17, 18-19 years), deprivation quintiles, ethnicity (White; Black; Asian; Mixed race; Other), and chronic condition status (yes/no) as recorded at the index admission, as possible confounding variables, or independent risk factors for death and re-admission, based on previous studies that have shown associations between these factors and harm in adolescents (258). More details on these groupings and how missing values were handled are provided in Section 3.3.5 (0.2% of adolescents had missing/inconsistent values for sex, 1.8% for deprivation, and 30.2% for ethnicity). ICD-10 codes used to define chronic conditions are described in Appendix C.4.

6.3.7 Statistical analyses

As in Study I, all analyses were carried out separately for girls and boys. I used time-to-event analysis methods (Kaplan-Meier [KM] estimates and semi-parametric proportional hazards [PH; ‘Cox’] regression), to account for the fact that the length of follow-up varied between adolescents (i.e. if the index admission occurred after March 31st 2002, their follow-up would be shorter than 10 years; and likely skewed), and that events (i.e., deaths and emergency re-admissions) could be censored (discussed further in Section 5.3).

Objective 3: To determine absolute risks of death and emergency re-admission in each cohort, I calculated KM probabilities, and 95% confidence intervals (CIs) for each age-group from one day to ten years after discharge from the index admission. I also calculated one-, five-, and ten-year risks of death and re-admission following 1) any violent, 2) any self-inflicted, and 3) any drug/alcohol related injury, to determine if risks differed according to type of adversity-related injury.

Objective 4: To compare risks of death in the adversity-related and accident-related injury groups, respectively, with those in the general population, I presented general population risk of death estimates for girls and boys, by age-group, alongside KM estimates. I derived general population estimates using freely available national statistics on risks of death in 10-19 year olds in 1997-1999 for the next 1-10 years in one-year increments (Appendix G.1) (259). A similar comparison of risks of re-admission would not be possible as, by definition, to be part of the general population an adolescent should not necessarily have an index emergency admission.

I tested for differences in risks of death and emergency re-admission over time between the adversity-related and accident-related injury groups, adjusting for potential confounding variables, using semi-parametric PH regressions, and presented hazard ratios (HRs) with 95% CIs. Models were adjusted in stages. I first estimated crude HRs between the two cohorts, and then estimated HRs adjusting for 1) age, 2) age and chronic condition status, and 3) age, chronic condition status, ethnicity and deprivation. Estimated HRs were attenuated after adjusting for age, (e.g., by 15.5% for death in girls). However, further adjustments for chronic condition status, ethnicity and deprivation did not substantially alter age-adjusted HRs, thus I present age-adjusted HRs as the main result.

From Study I (Chapter 4), we know that different types of adversity-related injury tend to co-occur at the same admission (212). Therefore, I also estimated age-adjusted HRs of death and emergency re-admission following the seven mutually exclusive combinations of violent, drug/alcohol-related, and self-inflicted injury (all versus accident-related injury), to determine if there were particular combinations where risks were different.

To determine whether there were additional risks of multiple emergency re-admissions for adolescents with adversity-related injury, I estimated age-adjusted HRs of a 2^{nd}, 3^{rd}, 4^{th}, and 5^{th} emergency re-admission (less than 5% of adolescents had more than five), using both the Wei, Lin & Weissfeld (WLW) and Prentice, Williams & Peterson gap-time (PWP-GT) approaches to modelling recurrent events in semi-parametric PH models (described in more detail in Section 5.8.2).

Model checks: I tested the PH assumption of semi-parametric PH models by plotting the observed KM survival curves against those predicted by the semi-parametric PH regressions. I also tested for the significance of an interaction term between adversity-related (vs. accident-related) injury with time and carried out the Schoenfeld residual test.

The overall goodness of fit of regression models was assessed by the plot of the observed KM survival curves against those predicted by the semi-parametric PH regressions, and by plotting the Nelson-Aalen estimate of the cumulative hazard function against Cox-Snell residuals and by employing the link test (221).

6.4 Results

There were 1,083,368 adolescents who had an emergency admission for injury (the study cohort). Of these adolescents, nearly one-third (n=333,009) formed the adversity-related injury group, and 60% (n=649,818) formed the accident-related injury group (Figure 6.2). The remaining 9% (e.g., those who died at the index admission, or were admitted with other causes of injury) were excluded from analyses.

There were similar numbers of girls and boys in the adversity-related injury group, but boys outnumbered girls by 2:1 in the accident-related injury group (girls: 166,462, boys: 484,356) (Figure 6.2). Compared with the accident-related injury group, adolescents in the adversity-related injury cohort were on average older at their index admission, and more likely to be from the most deprived areas or have a chronic condition (Table 6.1). The distribution of ethnicity did not differ substantially between the two groups.

The most common chronic conditions were chronic respiratory disorders (e.g., asthma), affecting 39.8% to 55.4% of the girls and boys with either adversity- or accident-related injury who also had a chronic condition (Table 6.2). Mental health or behavioural disorders (that were not already in the definition for "adversity") affected 33.0% to 33.5% of the girls and boys with an adversity-related injury and a chronic condition, but only 9.0% to 12.3% of the girls and boys who had an accident-related injury and a chronic condition.

In the adversity-related injury group, girls were admitted predominantly for drug/alcohol-related (90.1%) or self-inflicted (72.4%) injury, while boys were most often admitted for violent (46.7%) or drug/alcohol-related (56.5%) injury. The median follow-up time from the index admission ranged from 6.8 to 7.7 years in both groups (Table 6.3).

Table 6.1: Characteristics of adolescents at discharge from index emergency admission for injury (study cohort; England, April 1997-March 2012).

	Girls: n (%)		Boys: n (%)	
	Adversity-related injury	**Accident-related injury**	**Adversity-related injury**	**Accident-related injury**
All	181,926 (100.0)	166,462 (100.0)	151,083 (100.0)	483,356 (100.0)
10-14 years old	47,926 (26.3)	103,215 (62.0)	24,301 (16.1)	259,862 (53.8)
15-17 years old	84,605 (46.5)	36,624 (22.0)	57,706 (38.2)	137,044 (28.4)
18-19 years old	49,395 (27.2)	26,623 (16.0)	69,076 (45.7)	86,450 (17.9)
History of a chronic condition	47,310 (26.0)	34,357 (20.6)	34,782 (23.0)	90,963 (18.8)
Ethnicity:				
White	144,522 (79.4)	129,248 (77.6)	109,307 (72.3)	352,614 (73.0)
Black	4,284 (2.4)	3,320 (2.0)	4,486 (3.0)	9,917 (2.1)
Asian	6,432 (3.5)	4,066 (2.4)	4,563 (3.0)	13,633 (2.8)
Mixed	2,448 (1.3)	1,470 (0.9)	1,540 (1.0)	4,171 (0.9)
Other	3,309 (1.8)	2,541 (1.5)	3,000 (2.0)	7,491 (1.5)
Missing	20,931 (11.5)	25,817 (15.5)	28,187 (18.7)	95,530 (19.8)
Deprivation quintile:				
Least deprived	22,309 (12.3)	29,002 (17.4)	16,991 (11.2)	85,304 (17.6)
2nd least deprived	24,941 (13.7)	29,872 (17.9)	19,474 (12.9)	85,052 (17.6)
Middle quintile	30,698 (16.9)	30,472 (18.3)	24,450 (16.2)	87,512 (18.1)
2nd most deprived	40,721 (22.4)	32,670 (19.6)	33,461 (22.1)	95,821 (19.8)
Most deprived	61,161 (33.6)	41,923 (25.2)	53,437 (35.4)	122,749 (25.4)
Missing	2,096 (1.2)	2,523 (1.5)	3,270 (2.2)	6,918 (1.4)

Table 6.1 continued.

	Girls: n (%)		Boys: n (%)	
	Adversity-related injury	**Accident-related injury**	**Adversity-related injury**	**Accident-related injury**
All	181,926 (100.0)	166,462 (100.0)	151,083 (100.0)	483,356 (100.0)
Type of adversity-related injury				
Any violent injury	13,262 (7.3)	.	70,594 (46.7)	.
Any self-inflicted injury	131,739 (72.4)	.	44,621 (29.5)	.
Any drug/alcohol-related injury	163,888 (90.1)	.	85,421 (56.5)	.
Emergency admissions prior to index (at 10-19y old)				
Adversity-related injury	18,311 (10.1)	1,566 (0.9)	8,121 (5.4)	3,262 (0.7)
Accident-related injury (no adversity)	5,438 (3.0)	6,264 (3.8)	10,328 (6.8)	36,320 (7.5)

Table 6.2: Numbers of adolescents with different chronic health conditions, among study cohort

	Girls				Boys			
	Adversity-related injury		Accident-related injury		Adversity-related injury		Accident-related injury	
Total with history of a chronic condition	27,922	(100.0)	18,934	(100.0)	21,161	(100.0)	49,436	(100.0)
Type of chronic condition								
Mental health/behavioural	9,348	(33.5)	1,702	(9.0)	6,984	(33.0)	6,063	(12.3)
Cancer/blood disorders	677	(2.4)	799	(4.2)	693	(3.3)	2,049	(4.1)
Chronic infections	58	(0.2)	50	(0.3)	116	(0.5)	164	(0.3)
Respiratory	11,213	(40.2)	9,452	(49.9)	8,429	(39.8)	27,411	(55.4)
Metabolic/endocrine/digestive/renal/genitourinary	4,475	(16.0)	2,421	(12.8)	2,619	(12.4)	4,912	(9.9)
Musculoskeletal/skin	1,730	(6.2)	2,608	(13.8)	1,127	(5.3)	4,403	(8.9)
Neurological	4,537	(16.2)	4,708	(24.9)	4,063	(19.2)	9,804	(19.8)
Cardiovascular	266	(1.0)	273	(1.4)	232	(1.1)	656	(1.3)
Non-specific*	207	(0.7)	428	(2.3)	176	(0.8)	776	(1.6)

*Lack of expected normal physiological development, feeding difficulties and mismanagement, 'attention to gastronomy', palliative care, holiday relief care, 'gastrostomy status', dependence on wheelchair.

Table 6.3: Characteristics of deaths and emergency re-admissions within ten years following discharge from emergency admissions for adversity-related or accident-related injury during adolescence (England, April 1997-March 2012)

	Girls		Boys	
Variable, units	**Adversity-related injury**	**Accident-related injury**	**Adversity-related injury**	**Accident-related injury**
Number (column %)	181,926 (100.0)	166,462 (100.0)	151,083 (100.0)	483,356 (100.0)
Follow-up in years, Median (IQR)	6.8 (3.3, 10.0)	7.5 (3.9, 10.0)	7.0 (3.6, 10.0)	7.7 (4.1, 10.0)
Length of stay in days, Median (IQR)	1 (1, 1)	1 (1, 2)	1 (1, 2)	1 (1, 1)
Died, n (per 1,000)	873 (4.8)	439 (2.6)	1,542 (10.2)	1,928 (4.0)
Death related to injury, n (% who died)	688 (78.8)	166 (37.8)	1,226 (79.5)	1,314 (68.2)
Time to death in days, Median (IQR) b	1,247 (507, 2,227)	1,490 (709, 2,390)	1,196 (409, 2,162)	1,117 (468, 2,082)
Had an emergency re-admission, n (%)	77,101 (42.4)	44,790 (26.9)	46,284 (30.6)	108,812 (22.5)
1	34,846 (19.2)	25,479 (15.3)	26,008 (17.2)	75,160 (15.5)
2+	42,255 (23.2)	19,311 (11.6)	20,276 (13.4)	33,652 (7.0)
2	16,449 (9.0)	8,894 (5.3)	9,495 (6.3)	19,925 (4.1)
3-5	17,112 (9.4)	7,367 (4.4)	7,519 (5.0)	10,907 (2.3)
6+	8,694 (4.8)	3,050 (1.8)	3,262 (2.2)	2,820 (0.6)
for injury, n (% had emergency re-admission)	34,356 (44.6)	13,120 (29.3)	29,976 (64.8)	59,970 (55.1)
Total number of emergency re-admissions, n	227,385 .	102,095 .	108,839 .	182,731 .
for injury, n (% emergency re-admissions)	67,084 (29.5)	18,415 (18.0)	53,887 (49.5)	79,925 (43.7)
Median days to 1st emergency re-admission (IQR)	586 (179, 1,370)	930 (273, 1,898)	750 (220, 1,596)	933 (262, 1,907)
from 1st to 2nd	299 (75, 798)	347 (78, 926)	345 (91, 895)	430 (98,1,084)
from 2nd to 3rd	205 (50, 594)	214 (49, 592)	224 (58, 622)	256 (62, 687)

IQR = Inter-quartile Range
*Some adolescents were not followed up for the full ten years, e.g., adolescents admitted in 2011.

6.4.1 Objective 3: Absolute risks of death and emergency re-admission

There were 4,782 deaths within ten years of discharge (2,415 following adversity-related injury, 2,367 following accident-related injury) (Table 6.3). More than twice as many deaths occurred after discharge than occurred during hospitalisation for the index admission: 71.8% of all deaths between the index admission date and ten years later occurred post-discharge. The average time to death post-discharge in the two groups was 3.1 to 4.1 years. At ten years, the cumulative risk of death after hospital discharge in the adversity-related injury cohort was 7.3 per 1,000 for girls (equivalent to 1 in every 137) and 15.6 per 1,000 for boys (1 in every 64) (Appendix G.4).

There were 621,050 emergency re-admissions in both groups in total Table 6.3. On average, adolescents in the adversity-related injury group had their first emergency re-admission 586-750 days after discharge from the index admission, 6 to 12 months sooner than for the accident-related injury group. The ten-year risk of emergency re-admission was 54.2% for girls and 40.5% for boys (Appendix G.4).

6.4.2 Objective 4: Outcomes following adversity-related injury (versus accident-related injury)

Risks of death and emergency re-admission following discharge were higher following adversity-related injury than following accident-related injury at all time-points (Figure 6.3; Figure 6.4). For example, the ten-year risk of death following adversity-related injury for 10-14 year old girls was 4.8 per 1,000, and following accident-related injury was 2.8 per 1,000 (Appendix G.4). Comparing these risks to those in the general population, risks of death were also higher following adversity-related injury and marginally higher following accident-related injury. For a 10-14 year old girl in the general population in England in 1997-1999 the risk of death was 2.3 per 1,000.

For adolescents admitted with adversity-related and accident-related injury and all age-groups, boys had higher risks of death at all time-points when compared to girls. In contrast, girls had higher risks of emergency re-admission than boys at all time-points.

On average over the ten years following discharge, risks of death in the adversity-related injury cohort were 61% (95% CI: 43% to 82%) higher in girls and 113% (98% to 129%) higher in boys when compared with the accident-related injury cohort, after adjusting for age (Table 6.4; 95% CIs greater than unity). Risks of emergency re-admission were 76% greater for girls in the adversity-related injury cohort compared to those in the accident-related injury cohort (95% CI: 74% to 79%), and 41% greater for boys (39% to 43%).

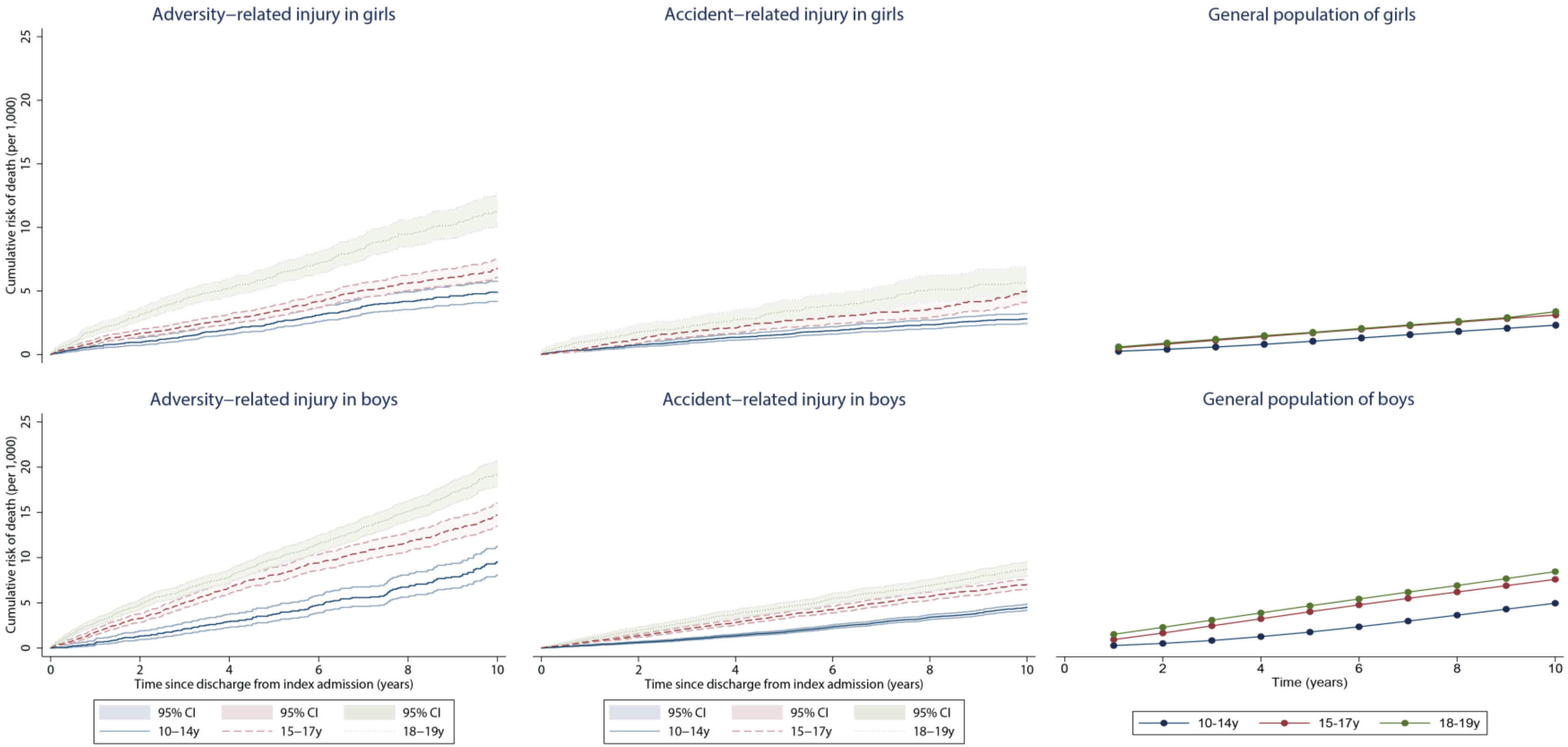


Figure 6.3: Cumulative risks of death following discharge from index admissions for adversity-related and accident-related injury, and for the general population of adolescents

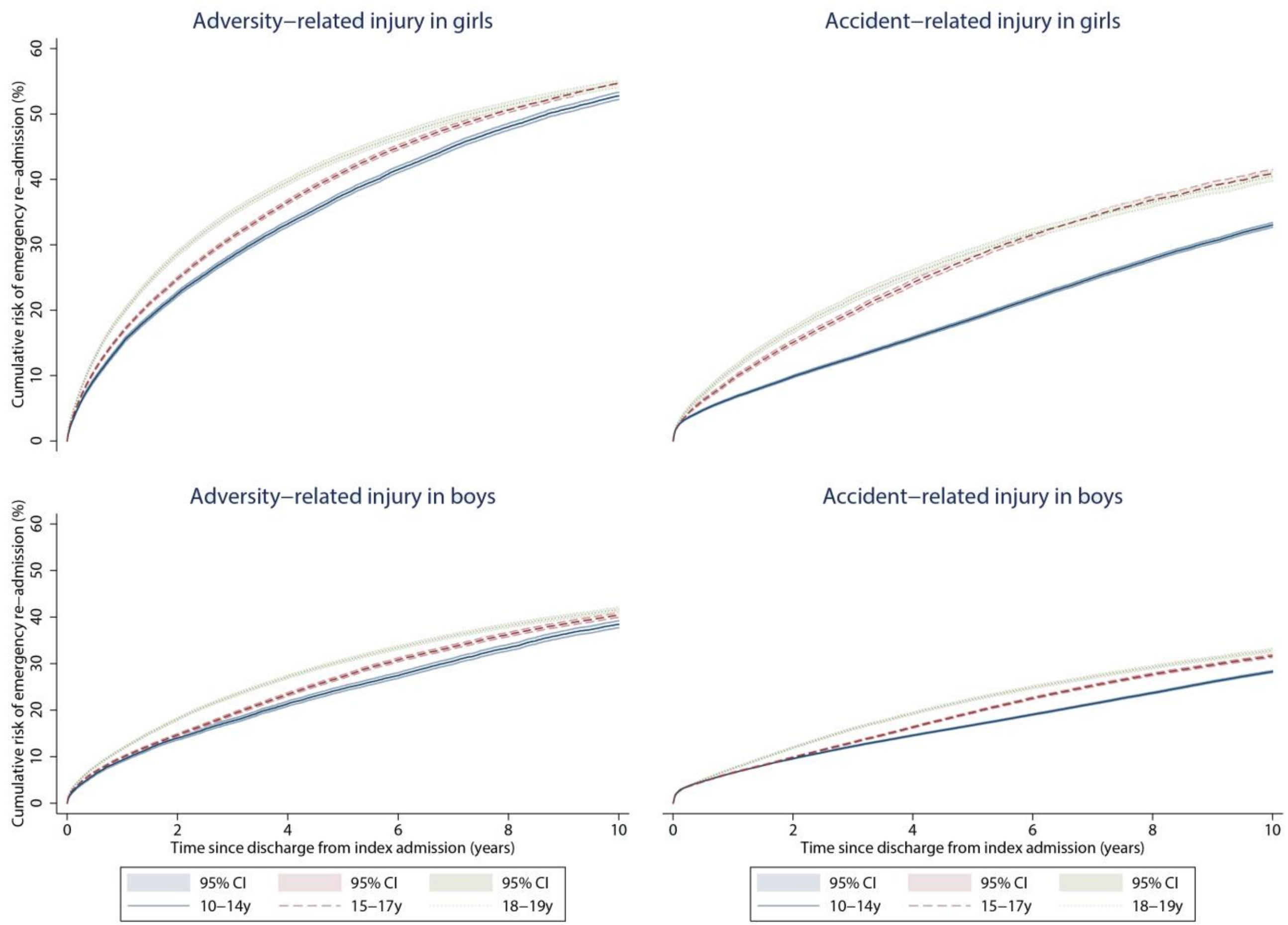


Figure 6.4: Cumulative risks of emergency re-admissions following discharge from index admissions for adversity-related and accident-related injury

Table 6.4: Relative risks of death and emergency re-admission within ten years of discharge from index admission

Sex Variable at index	Hazard Ratio* (95% Confidence Interval)	
	Death	Emergency re-admission
Girls		
Adversity-related (vs. Accident-related) injury	1.61 (1.43 to 1.82)	1.76 (1.74 to 1.79)
Age-group (vs. 10-14 years)		
15-17 years	1.46 (1.27 to 1.69)	1.22 (1.20 to 1.23)
18-19 years	2.32 (2.01 to 2.68)	1.29 (1.27 to 1.31)
Boys		
Adversity-related (vs. Accident-related) injury	2.13 (1.98 to 2.29)	1.41 (1.39 to 1.43)
Age-group (vs. 10-14 years)		
15-17 years	1.68 (1.54 to 1.84)	1.14 (1.13 to 1.15)
18-19 years	2.16 (1.98 to 2.37)	1.26 (1.24 to 1.27)

*Hazard ratios estimated from semi-parametric proportional hazards models where the independent variables were adversity-related/accident-related injury and age-group (both entered into the same model). One model fitted for each combination of sex and outcome.

Ten-year risks of death were significantly higher following all types of adversity-related injury compared with accident-related injury, particularly following self-inflicted injury in 18-19 year old girls (>10 per 1,000), 15-17 and 18-19 year old boys (>20 per 1,000 and >30 per 1,000, respectively) (Figure 6.6). Ten-year risks of emergency re-admissions were also higher following all types of adversity-related injury compared with accident-related injury (Figure 6.6). In older boys (15-17 and 18-19 years), risks of emergency re-admissions were highest following self-inflicted injury.

Risks of death were increased in girls and boys following all combinations of violent, self-inflicted, and drug/alcohol-related injury, compared with accident-related injury (Figure 6.7; age-adjusted HRs ranged from 1.09 to 5.35). These risks were particularly increased following combinations of adversity-related injury that included drug/alcohol-related injury (age-adjusted HRs ranged from 1.61 to 5.35), although this was not statistically significantly increased following admissions with records of all three types in girls (age-adjusted HR: 2.43, 95% CI: 0.91 to 6.51).

Similarly, risks of emergency re-admission following all combinations of types of adversity-related injury were increased compared with accident-related injury (Figure 6.8; age-adjusted HRs ranged from 1.33 to 3.10). Risks were particularly increased following combinations including self-inflicted or drug/alcohol-related injury (e.g., age-adjusted HR of death for boys with self-inflicted and drug/alcohol-related injury [vs. accident-related injury]: 3.41, 95% CI: 3.11 to 3.74).

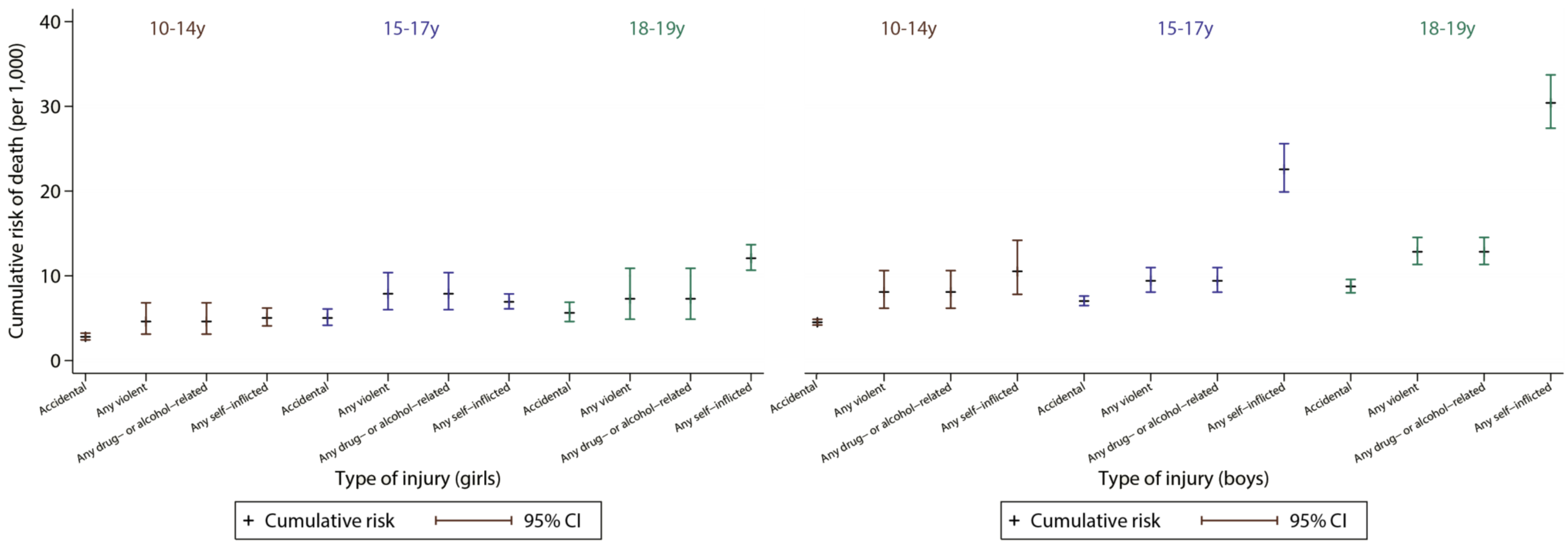


Figure 6.5: Ten-year risks of death, by type of injury at index

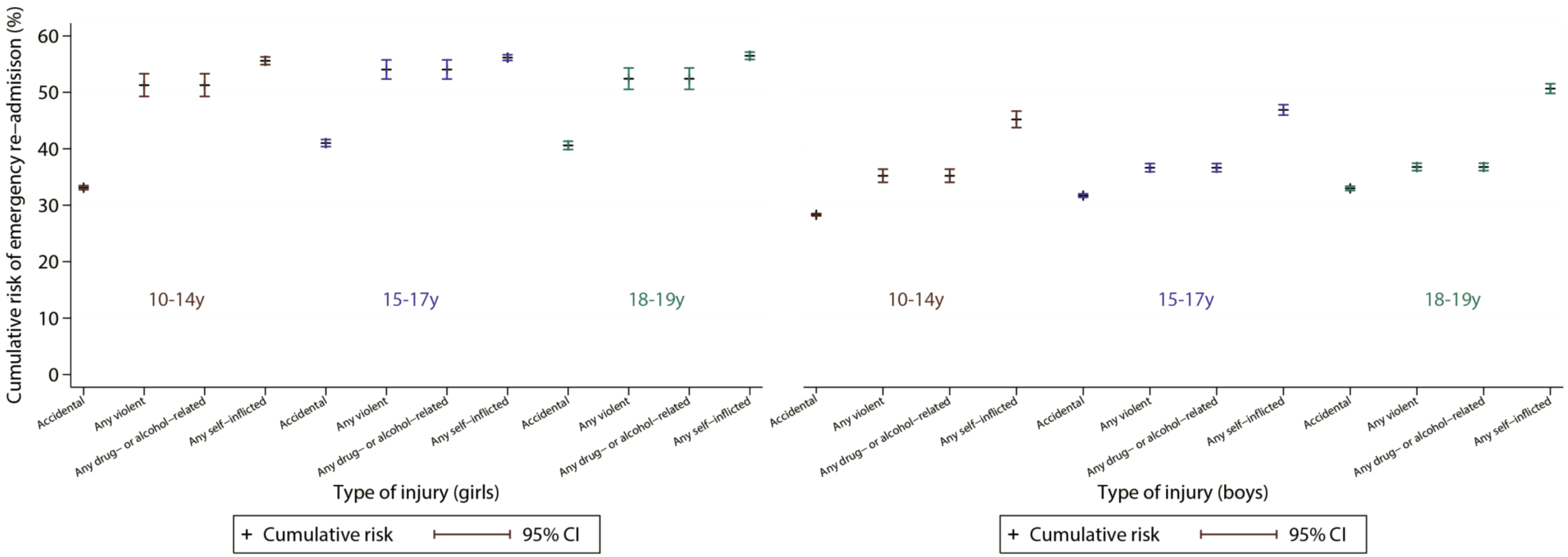


Figure 6.6: Ten-year risks of emergency re-admission, by type of injury at index

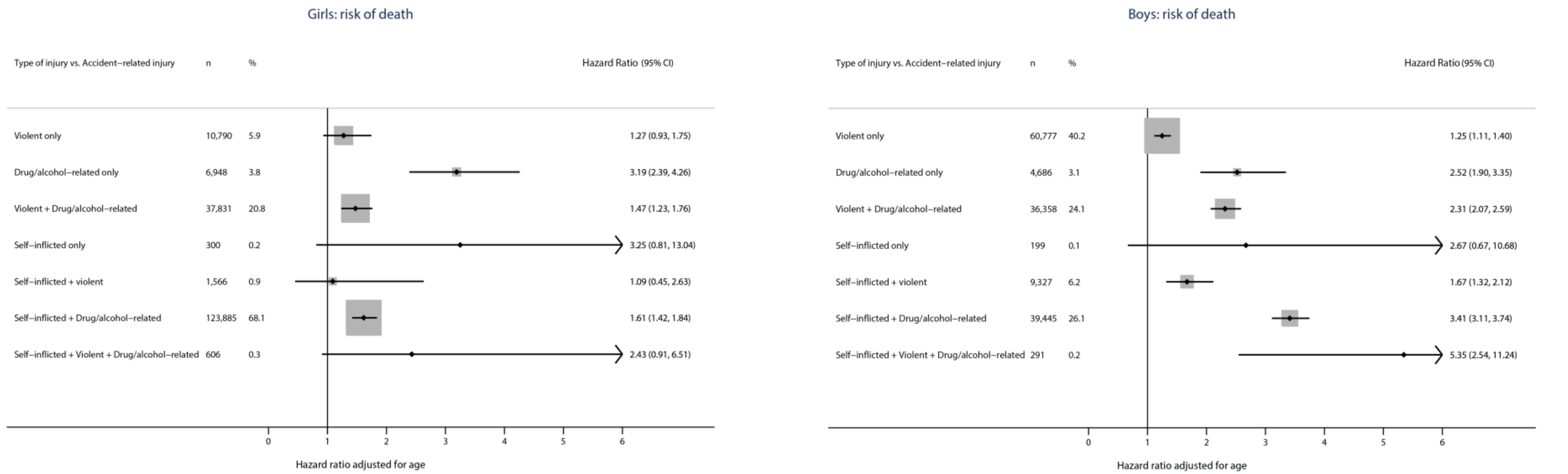
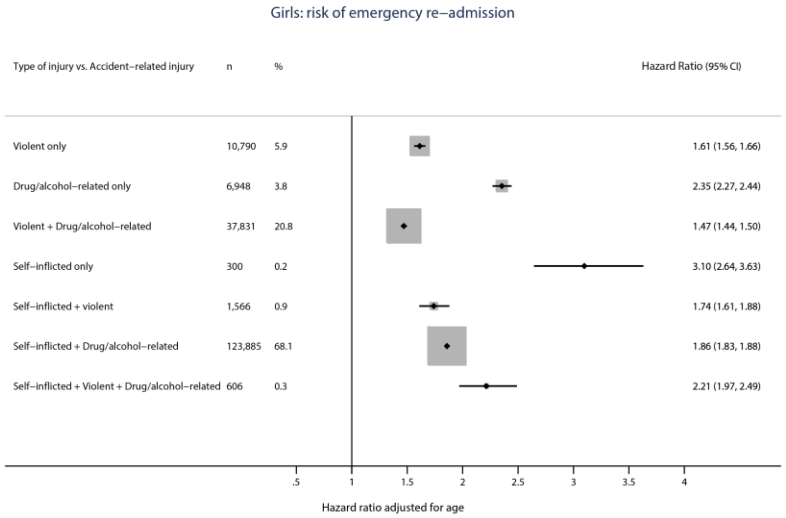


Figure 6.7: Relative risks of death, by combination of different types of adversity-related injury (vs. accident-related injury)



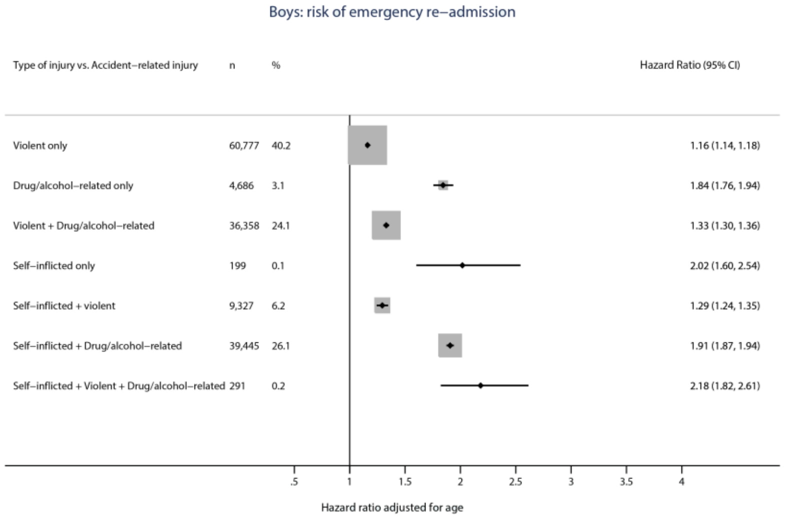


Figure 6.8: Relative risks of emergency re-admission, by combination of different types of adversity-related injury (vs. accident-related injury)

Results outlining the risk of death among girls and boys, using models adjusted for other variables identified *a priori*, are presented in Table 6.5 and Table 6.6. After adjusting for age-group, HRs changed little with further adjustment for chronic condition status, ethnicity and deprivation. Presence of a chronic condition increased risks of death by nearly four-fold. There were no apparent relationships between ethnicity and risks of death. Girls and boys in the most deprived quintiles had the highest risks of death (compared to other those in other quintiles), but these associations were not statistically significant. Missing information on deprivation was associated with reduced risks of death, possibly due to failure to link between HES and ONS data for individuals with incomplete data (260). When models for emergency re-admissions in girls and boys were adjusted in the same way, very similar relationships were observed as above for girls and death (Appendix G.5).

Table 6.5: Relative risks of death within ten years of discharge from index admission for girls, by adjustment for potential confounding factors

Girls: death	Hazard ratio (95% Confidence Interval)			
Variables at index	**Unadjusted**	**Adjusted for age**	**Adjusted for age, chronic condition status**	**Adjusted for age, chronic condition status, ethnicity, deprivation**
Adversity-related (vs. Accident-related) injury	1.93 (1.72, 2.16)	1.61 (1.43, 1.82)	1.51 (1.34, 1.71)	1.48 (1.31, 1.68)
Age-group (vs. 10-14 years):				
15-17 years	. .	1.46 (1.27, 1.69)	1.40 (1.21, 1.61)	1.41 (1.22, 1.62)
18-19 years	. .	2.32 (2.01, 2.68)	2.10 (1.82, 2.42)	2.10 (1.82, 2.42)
Chronic condition (vs. None)	. .	. .	3.77 (3.38, 4.20)	3.72 (3.33, 4.15)
Ethnicity (vs. White):				
Black	. .	. .	. .	1.01 (0.70, 1.47)
Asian	. .	. .	. .	1.09 (0.81, 1.48)
Mixed	. .	. .	. .	0.61 (0.30, 1.22)
Other	. .	. .	. .	0.68 (0.40, 1.14)
Missing	. .	. .	. .	0.96 (0.80, 1.14)
Deprivation quintile (vs. Least deprived):				
2nd least deprived	. .	. .	. .	1.05 (0.85, 1.30)
Middle quintile	. .	. .	. .	1.05 (0.85, 1.28)
2nd most deprived	. .	. .	. .	1.18 (0.97, 1.43)
Most deprived	. .	. .	. .	1.22 (1.02, 1.47)
Missing	. .	. .	. .	0.22 (0.07, 0.70)

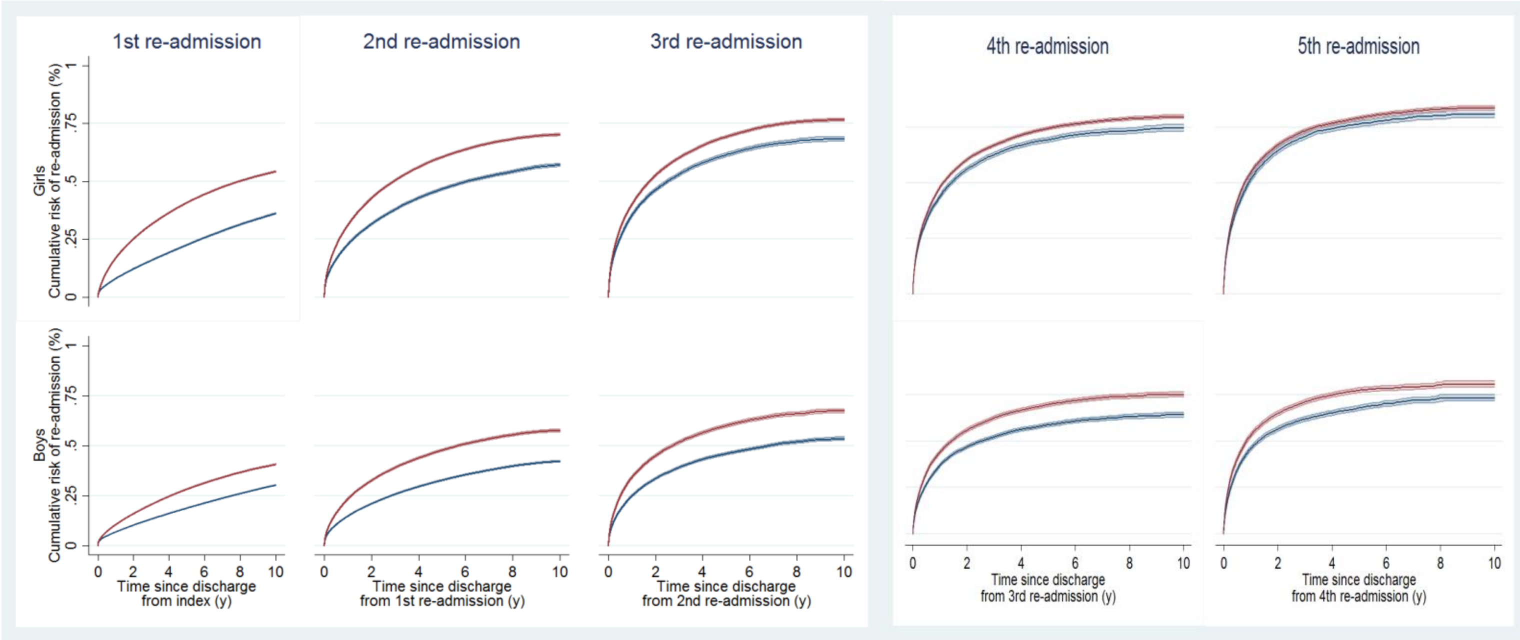
All variables were entered simultaneously into a semi-parametric proportionak hazards model (multi-variable results).

Table 6.6: Relative risks of death within ten years of discharge from index admission for girls, by adjustment for potential confounding factors

Boys: death	**Hazard ratio (95% Confidence Interval)**			
Variables at index	**Unadjusted**	**Adjusted for age**	**Adjusted for age, chronic condition status**	**Adjusted for age, chronic condition status, ethnicity, deprivation**
Adversity-related (vs. Accident-related) injury	2.70 (2.53, 2.89)	2.13 (1.98, 2.29)	2.02 (1.88, 2.17)	1.94 (1.80, 2.08)
Age-group (vs. 10-14 years):				
15-17 years	. .	1.68 (1.54, 1.84)	1.72 (1.57, 1.88)	1.73 (1.58, 1.89)
18-19 years	. .	2.16 (1.98, 2.37)	2.22 (2.03, 2.43)	2.23 (2.04, 2.44)
Chronic condition (vs. None)	2.66 (2.49, 2.85)	2.58 (2.41, 2.77)	2.66 (2.49, 2.85)	2.58 (2.41, 2.77)
Ethnicity (vs. White):				
Black	. .	. .	. .	1.05 (0.85, 1.31)
Asian	. .	. .	. .	0.89 (0.72, 1.10)
Mixed	. .	. .	. .	0.76 (0.49, 1.18)
Other	. .	. .	. .	0.74 (0.55, 1.00)
Missing	. .	. .	. .	0.85 (0.78, 0.93)
Deprivation quintile (vs. Least deprived):				
2nd least deprived	. .	. .	. .	1.24 (1.08, 1.42)
Middle quintile	. .	. .	. .	1.28 (1.12, 1.46)
2nd most deprived	. .	. .	. .	1.42 (1.25, 1.61)
Most deprived	. .	. .	. .	1.62 (1.44, 1.83)
Missing	. .	. .	. .	0.57 (0.38, 0.87)

Risk of multiple emergency re-admissions

Among the adversity-related injury group, 13.4% of girls and 23.2% of boys had two or more emergency re-admissions, compared to 11.6% and 7.0% in the accident-related injury group (Table 6.3). Risks of a second, third, fourth and fifth emergency re-admission were increased in the adversity-related injury cohort at all time-points after the index admission (Figure 6.9). When WLW and PWP gap-time models were each fitted to adjust for differences in age between the two groups, both models indicated increased risks of higher order emergency re-admissions following adversity-related injury (Table 6.7). For example, for adolescent girls who had already had a first emergency re-admission, if they had originally been admitted with adversity-related injury, their risk of a second emergency re-admission was 38% greater than if they had originally been admitted with accident-related injury. As one would expect, relative risks estimated via the WLW approach were larger than those estimated via the PWP-gap-time approach (reasons for this are discussed in Section 5.8.2).



Kaplan-Meier estimates of cumulative risk presented, with 95% CIs shaded. Red = Adversity-related injury, Blue = Accident-related injury.

Figure 6.9: Cumulative risks of a subsequent emergency re-admission, for adolescents who already had a 1st, 2nd, 3rd and 4th re-admission

Table 6.7: Relative risks of first-fifth emergency re-admissions* within ten years following discharge from index admission

Sex Model	Order of emergency re-admission after discharge from index Age-adjusted HR for adversity-related vs. accident-related injury (95% Confidence Interval)					
	First	**Second**	**Third**	**Fourth**	**Fifth**	**Overall**
Girls						
WLW	1.76 (1.74, 1.79)	2.09 (2.05, 2.13)	2.26 (2.21, 2.32)	2.35 (2.28, 2.43)	2.38 (2.29, 2.46)	1.97 (1.96 to 2.00)
PWP Gap time	1.76 (1.74, 1.79)	1.38 (1.35 to 1.40)	1.18 (1.15 to 1.20)	1.10 (1.07 to 1.13)	1.05 (1.01 to 1.09)	1.49 (1.47 to 1.50)
Boys						
WLW	1.41 (1.39, 1.43)	1.87 (1.83, 1.90)	2.29 (2.23, 2.36)	2.64 (2.55, 2.74)	2.94 (2.81, 3.07)	1.68 (1.67 to 1.70)
PWP Gap time	1.41 (1.39, 1.43)	1.49 (1.47 to 1.50)	1.36 (1.33 to 1.40)	1.25 (1.20 to 1.29)	1.22 (1.16 to 1.27)	1.40 (1.39 to 1.41)

*Time to each emergency re-admission was defined as the time since discharge from the index admission.
WLW = Wei, Lin & Weissfeld; PWP = Prentice, Williams & Peterson
Semi-parametric proportional hazards models.

Model checks

Plots of observed KM and predicted survival curves did not indicate deviation from the PH assumption between adversity-related and accident-related injury among girls where the outcome was death (Appendix G.2). Neither did the interaction term of adversity-related injury with time (p=0.234) nor the Schoenfeld residual test (p=0.336) (Appendix G.3). However, there was some indication of deviation from the PH assumption for girls when the outcome was emergency re-admission, and for boys when the outcome was either death or emergency re-admission (Appendices G.2 and G.3).

According to the plots of observed KM and predicted survival curves, Cox-Snell plots, and the link test, models for girls and boys where the outcome was death, and boys where the outcome was emergency re-admission, provided an adequate goodness-of-fit (Appendices G.3 and G.4). However, they also indicated that the model for girls where the outcome was emergency re-admission may not have.

6.5 Discussion

One in 137 girls and one in 64 boys died in the ten years after being admitted to hospital for adversity-related injury; 54.2% and 40.5% had an emergency re-admission. Risks of death were particularly increased for older adolescent boys: 1 in 52 died in the ten years after discharge. Risks of death and emergency re-admission in the ten years after discharge from an emergency admission for adversity-related injury during adolescence were approximately double that following an emergency admission for accident-related injury. These risks were increased following all types of adversity-related injury. Chronic conditions independently increased risks by two to four-fold.

6.5.1 Strengths and limitations

These are the first all-cause long-terms risks of harm to be estimated in adolescents seen in hospital with any adversity-related injury. Previously, risks have been estimated for each type of adversity-related injury in a different group of patients each time (described in greater detail in Section 1.5). This is also the first study to have presented risks of harm in adolescents hospitalised with adversity, compared to those for other hospitalised adolescents.

A strength of this study is that it was carried out in a large dataset, where outcomes were objectively measured. Linked admissions within HES and linked ONS mortality data are likely to have picked up the majority of outcomes over the course of the next ten years. Carrying out this study in such an established administrative dataset has allowed long-term follow-up that has not been possible in previous cohort studies of hospitalised adolescents (Section 1.4).

I took a pragmatic approach to my choice of statistical methods for this study. I considered these methods alongside alternatives (see Chapter 5). For example, for comparing risks of death or re-admission between adolescents admitted with adversity-related injury and those admitted with accident-related injury, I chose to estimate these risks through semi-parametric PH modelling. I did consider parametric models that could have induced more efficient estimates, but there were no distributions that well matched the observed event time. Despite some evidence of deviation from the PH assumption for some of the models in this study, most other statistical tests nevertheless indicated an adequate goodness-of-fit.

One limitation is potential misclassification of violent, drug/alcohol-related, or self-inflicted injury as accident-related injury (191, 194). This misclassification would result in under-estimated risk differences between violent, drug/alcohol-related, or self-inflicted injury, and accident-related injury. Furthermore, linkage error (specifically 'missed-matching') is more prevalent among certain ethnic minorities or deprived individuals (260)(203). This was likely to lead to underestimation of the risks of death and re-admission for these groups. These issues are discussed in further detail in Section 3.3.6.

6.5.2 Comparisons with other studies

Mortality rates in this study were either similar or slightly higher than those reported for adolescent populations presenting with, but not necessarily admitted with, adversity-related injury. Unlike the current study, the groups of patients studied were not nationally representative. One-year risks of all-cause death following violent injury in our data (girls: 0.5, boys: 1.2 per 1,000) were comparable to *two*-year risks of violent injury death following violent and drug/alcohol-related injury presentations (including non-admissions) in 14-24 year olds at a US hospital (0.8 per 1,000) (91). In the current study, five-year risks of death following self-inflicted injury (girls: 4.0, boys: 12.7 per 1,000) were similar to reported mortality risks following self-harm presentations from 10-18 year olds in England over a median follow-up of six years (10 per 1,000, maximum follow-up 11 years) (90).

The estimated risks of emergency re-admission within one year of discharge were comparable to those reported for violent re-injury within *two* years of a drug/alcohol-related injury presentation in 14-24 year olds in the US (91), and those reported for repeat self-inflicted injury within one year of a self-inflicted injury presentation in 10-18 year olds in England (90). We could not find any other comparable studies of risks of re-admission past two years after discharge.

6.5.3 Implications of findings

Risks of death and emergency re-admission are substantially increased in the decade following an emergency admission for adversity-related injury, compared to those in the general population or to those following accident-related injury. Interventions that can be delivered to this group close to the time of discharge, and that are effective for reducing risks of future harm, are needed.

In Study I, it was shown that several adolescents admitted with adversity-related injury are admitted with multiple types, and thus related national clinical guidelines should reflect this (e.g., guidelines for managing adolescents seen with violent injury should be developed). The finding from this current study that adolescents admitted with violent injury are at just as much risk of subsequent death and re-admission in the next decade further supports this proposal. The fact that the risk of death consistently increased across the following decade showing no sign of decelerating indicates that intervention has the potential to impact on outcomes throughout the rest of adolescence and into young adulthood. Policymakers and practitioners need to seize this moment to reduce risks of future harm.

The current study provides a set of risk-factors for clinicians to identify adolescents at highest risks of future harm. Clinicians can expect girls to be more likely to be re-admitted following an adversity-related injury than boys, but boys to be more likely to die. This may also inform the type of intervention that is delivered (e.g., attempting to follow-up boys and keep contact after discharge). Those who were older, had an underlying chronic condition, or were from deprived areas, and those exposed to multiple types adversity (e.g., drug/alcohol misuse and self-harm) had the highest risks of future harm. These adolescents can be identified, but as shown in the overview of systematic reviews in Section 1.6, we still need evidence of the effectiveness, feasibility, and cost-effectiveness of interventions for adolescents hospitalised with adversity-related injury in a UK setting.

Since risks of all-cause death and all-cause emergency re-admissions amongst individuals admitted to hospital were increased following admission for adversity-related injury, those evaluating interventions to reduce harm need to consider broad outcomes. Section 1.6 also illustrates that to date, most trials of interventions to reduce harm in this adolescent group have only considered the incidence of repeat injury of the same type as at index. Further work on the causes of death and emergency re-admission in the ten years after discharge, following an admission for adversity-related injury compared to following accident-related injury, will give insights as to which cause, other than repeat injury (for the same reason as at the index admission), are driving these surplus deaths and admissions.

Chapter 7 Study III, Pathways from adversity-related injury to increased risks of death (Objective 5)

7.1 Chapter summary

This describes the methods for addressing Objective 5, followed by the corresponding findings and interpretation. This objective was to estimate cause-specific risks of death in the ten years following admissions for adversity-related injury during adolescence, and to compare these risks to those following accident-related injury.

Using the same data and cohort as in Study II (Chapter 6), I estimated cause-specific risks of death (adversity-related [homicide, suicide, drug/alcohol-related deaths], accidental and other; defined by ICD-9 and -10 codes), over the ten years after discharge from an admission for adversity-related or accident-related injury, as cumulative incidence functions (CIFs; which are described in Section 5.6.1). I compared cause-specific risks between adversity-related and accident-related injury, using Fine & Gray subhazard models (the form of these models are described in Section 5.6.1), whilst adjusting for differences in age-groups and chronic condition status. CIFs and Fine & Gray models accounted for the 'competing risks' of other remaining causes (e.g., when the event of interest was homicide, these methods were used to estimate risks of homicide, whilst accounting for competing risks of suicide, drug/alcohol-related deaths, etc.).

There were 4,782 deaths in the study cohort. The increased risks of death following all types of adversity-related injury (reported in Study II, Chapter 6) were accounted for by increased risks of suicide and drug/alcohol-related injury among girls and boys (adjusted risks were increased by 3.3 to 4.9 times, 95% CIs ranged from 2.9 to 7.0), and increased risks of accidental deaths for boys (by 1.3 times; 95% CI: 1.1 to 1.5). Following all types of adversity-related injury and accident-related injury, ten-year risks of drug/alcohol-related deaths were similar to those for suicide (e.g., for girls admitted with self-inflicted injury, ten-year risk of suicide: 2.9/1,000, drug/alcohol-related death: 2.7/1,000).

The findings of Study III suggest that guidelines, policies and evaluations of interventions, to reduce risks of future harm in adolescents who present with adversity-related injury, should encompass a range of adverse outcomes, not just a repeat of the index incident itself (e.g., suicide following self-inflicted injury). The results also highlight the burden of drug/alcohol-related deaths in this group, which is shown to be equal to that of suicide (each accounted for approximately one third of deaths in this group). Current guidelines and policy for reducing harm after any adversity in adolescents, particularly self-inflicted injury, currently focus on assessing risks of suicide when deciding when to admit individuals. They could be developed to increase the focus on risks of drug/alcohol-related deaths.

7.2 Introduction

In Chapter 5, it was shown that among adolescents admitted to hospitals as an emergency with adversity-related injury (violent, self-inflicted or drug/alcohol-related injury), approximately 1 in 137 girls and 1 in 64 boys could be expected to be dead (from any cause) in the ten years after discharge (256). These risks were approximately double that compared with adolescents admitted for accident-related injury. Therefore intervention to reduce risks of harm in this group could impact on outcomes into the next decade. However, it is unclear as to the ideal format for an effective intervention (e.g., Brief Motivational Interview, youth-worker, etc.; discussed in Section 1.6).

There is a need to understand the typical pathways from discharge after an admission for adversity-related injury to an increased risk of death. For example, interventions to reduce harm following self-inflicted injury focus on preventing suicide, but these adolescents may also be at increased risks of death for other reasons, caused by a drift towards other risk-taking behaviours. In a cohort of 15-24y olds presenting to a hospital in Oxford with self-harm in 1978-1997, over a median of 11y later there were increased risks of not only suicide when compared to the general population, but of death from respiratory and circulatory disorders and accidents (82). There are no similarly published estimates of risks following violent or drug/alcohol-related injury.

In the current study, I used the HES-ONS dataset to address Objective 5 of this thesis:

5. To quantify the risks of cause-specific death (homicide, suicide, drug/alcohol-related, accidental, other) following adversity-related injury and compare these risks to those following accident-related injury.

The main results from this chapter form part of a journal article that is currently under review with *The Lancet*.

7.3 Methods

7.3.1 Study cohort

In this study, I analysed data on the same cohort as for Study II (Chapter 5), using the anonymised HES-ONS data extract (April 1997-March 2012). This cohort is described in detail in Section 6.3.4. Briefly, this cohort was of 333,009 adolescents who were admitted as an emergency with adversity-related injury (181,926 girls, 151,083 boys), and 649,818 who were admitted as an emergency with accident-related injury (166,462 girls, 483,356 boys) (Figure 6.2). Adolescents who, during the index admission, did not have sex recorded (n=885; 0.08%), died (n=1,877; 0.17%), had an invalid or no discharge date (n=372; 0.03%), or did not have adversity-related nor accident-related injury (n=94,407; 8.9%) were excluded from analyses. For adolescents admitted with adversity-related injury, most girls had self-inflicted (72.4%) or drug/alcohol-related injury (90.1%), and most boys had violent (46.7%) or drug/alcohol-related injury (56.5%).

7.3.2 Exposures and other characteristics

The ICD-10 codes within admission records that were used to define the exposures (adversity-related, accident-related, violent, self-inflicted, and drug/alcohol-related injury) are described in Section 4.3.

I included age-group and chronic conditions in analyses, as it was found in Study II (Chapter 6) that these factors were associated with risks of death for the cohort independent of adversity-related and accident-related injury.

Age was grouped slightly differently compared to in Studies I and II (where age was grouped as 10-14, 15-17 and 18-19 years), due to discussions (which took place post-Study II) between collaborators on Study III. We decided that re-grouping age as 10-15, 16-17 and 18-19 years would better reflect different age-related recommendations in national guidelines for management of self-harm or alcohol misuse (57, 58, 64). For example, it is currently mandatory that all adolescents under 16 years of age who present with self-inflicted injury, be admitted (58). However, for those 16 years or older, this admission is at the clinician's discretion, and so patterns of admission for adversity-related injury and subsequent outcomes may differ.

The definition of chronic condition status according to ICD-10 codes is discussed in detail in Section 3.3.5.

7.3.3 Outcome measures

The outcome of interest was cause-specific death between one day after discharge from the index admission and up to ten years later. I identified deaths using linked Office for National Statistics (ONS) mortality data from death certificates (as in Study II). I identified cause of death from fields in the mortality data for the underlying cause and fields for up to 15 other contributing causes, that were recorded as ICD-9 and ICD-10 codes. I then categorised causes as clusters of these codes (described in Appendix C.3). Causes were categorised as one of three non-mutually exclusive types of death:

1) 'adversity-related' (homicide, suicide, and drug/alcohol-related deaths; these three sub-types were also mutually exclusive)
2) 'accidental' (no codes for adversity-related death, but codes for accidental causes)

3) ‘other causes’ (no codes for adversity-related or accidental death) (180).

Undetermined causes of death (E980-E989, Y1-Y34; n=483) were categorised under suicide, and an adjourned inquest (U50.9; n=130) was categorised as homicide, as advised by the ONS (169).

7.3.4 Statistical analyses

As for Studies I and II, all analyses were carried out separately for girls and boys. As part of the agreement with NHS Digital for data release (to not publish any counts <10), I do not present exact numbers of homicides for certain groups.

I determined absolute numbers of cause-specific deaths in the ten years post-discharge (and as proportions of total deaths) for adolescents with adversity-related, accident-related, violent, self-inflicted, and drug/alcohol-related injury, respectively.

Objective 5: To quantify risks of cause-specific death and compare these risks between adolescents admitted with adversity-related and accident-related injury, I used ‘competing risks’ statistical methods (Cumulative Incidence Functions [CIFs] with 95% CIs, and Fine & Grays subhazard models) (221, 237). The methods can be used to estimate and compare cause-specific risks of death (e.g., homicide) whilst controlling for the underlying risks of other (defined) competing risks (e.g., those for suicide, drug/alcohol-related deaths, etc.). These methods are described in more detail in Section 5.6.1.

I plotted cumulative risks for each cause (stacked CIF plots) (221), over the ten years after discharge from adversity-related and accident-related injury, respectively. To determine whether risks of cause-specific deaths differed after violent, self-inflicted, and drug/alcohol-related injury, I explicitly present 10y cumulative risks after discharge from each of these types of injury. Since in Study II 10y risks of all-cause death were shown to vary by age-group, I also present 10y cause-specific risks in a supplementary table.

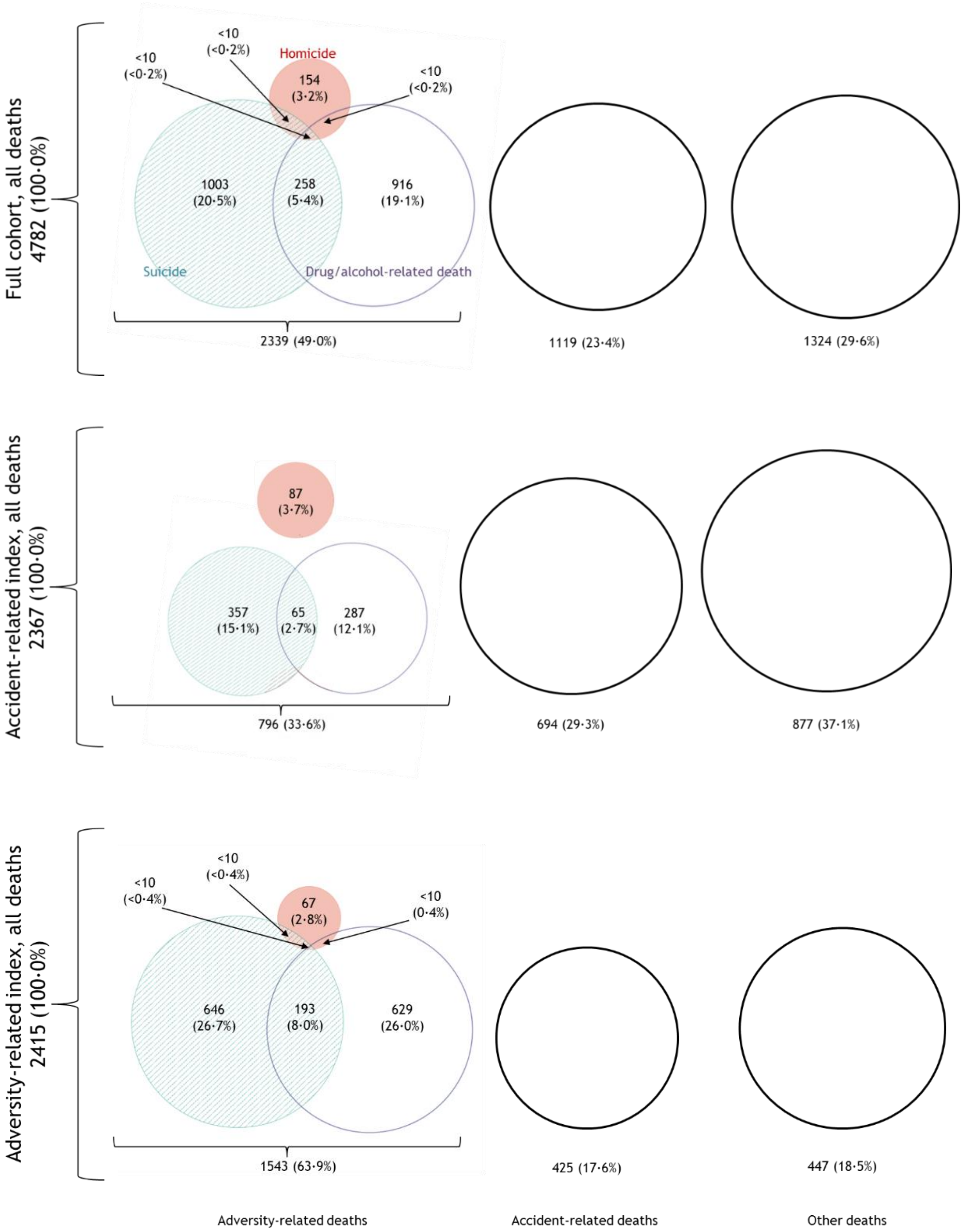
Finally, to compare risks between adversity-related and accident-related injury whilst adjusting for other covariates I fitted Fine & Gray models. The outputs of these models are 'sub-hazard ratios' (SHRs), which for each independent variable in the model, represent the corresponding multiplicative change in risk of death through the specific cause in question, compared to the baseline category (and adjusted for the other independent variables). We fitted a separate model with each cause-specific death as the dependent variable, and adversity-related (vs. accident-related) injury, age-group and chronic condition status as independent variables.

Model checks: To test the assumption of proportional sub-distribution hazards of adversity-related (vs. accident-related) injury, I tested for a non-zero slope of Schoenfeld residuals and a non-zero coefficient for adversity-related (vs. accident-related) injury as a time-varying covariate. To test the goodness-of-fit of models, I used the link test (221).

7.4 Results

For adolescents admitted with either adversity-related or accident-related injury, there was a total of 4,782 deaths post-discharge (girls: 1,312, boys: 3,470, Table 7.1). Nearly half of these deaths were adversity-related (2,339, 49.0%; Figure 7.1), of which the majority were related to suicide or drug/alcohol use (suicide only: 20.5%, drug/alcohol-related only: 19.1%, both: ~5.4%).

Among all adversity-related deaths, 8.0% also had record of an accident in the death certificate (data not shown). Of the 1,119 accidental deaths, 60.0% were related to transport accidents. Among the 1,531 deaths through other causes, the most common causes were related to neurological (32.5%) or cancer/blood disorders (24.5%; of nine possible groups of ICD codes relating to systems within the body (180, 261).



Circles represent proportions and are drawn to scale. Accidental death: codes for accidents and no codes for adversity in death certificate; Other death: no codes for accidents or adversity in death certificate.

Figure 7.1: Numbers and proportions of cause-specific deaths, for the full cohort and by type of injury at index admission.

Table 7.1: Numbers and proportions of cause-specific deaths, by sex and type of injury at index admission

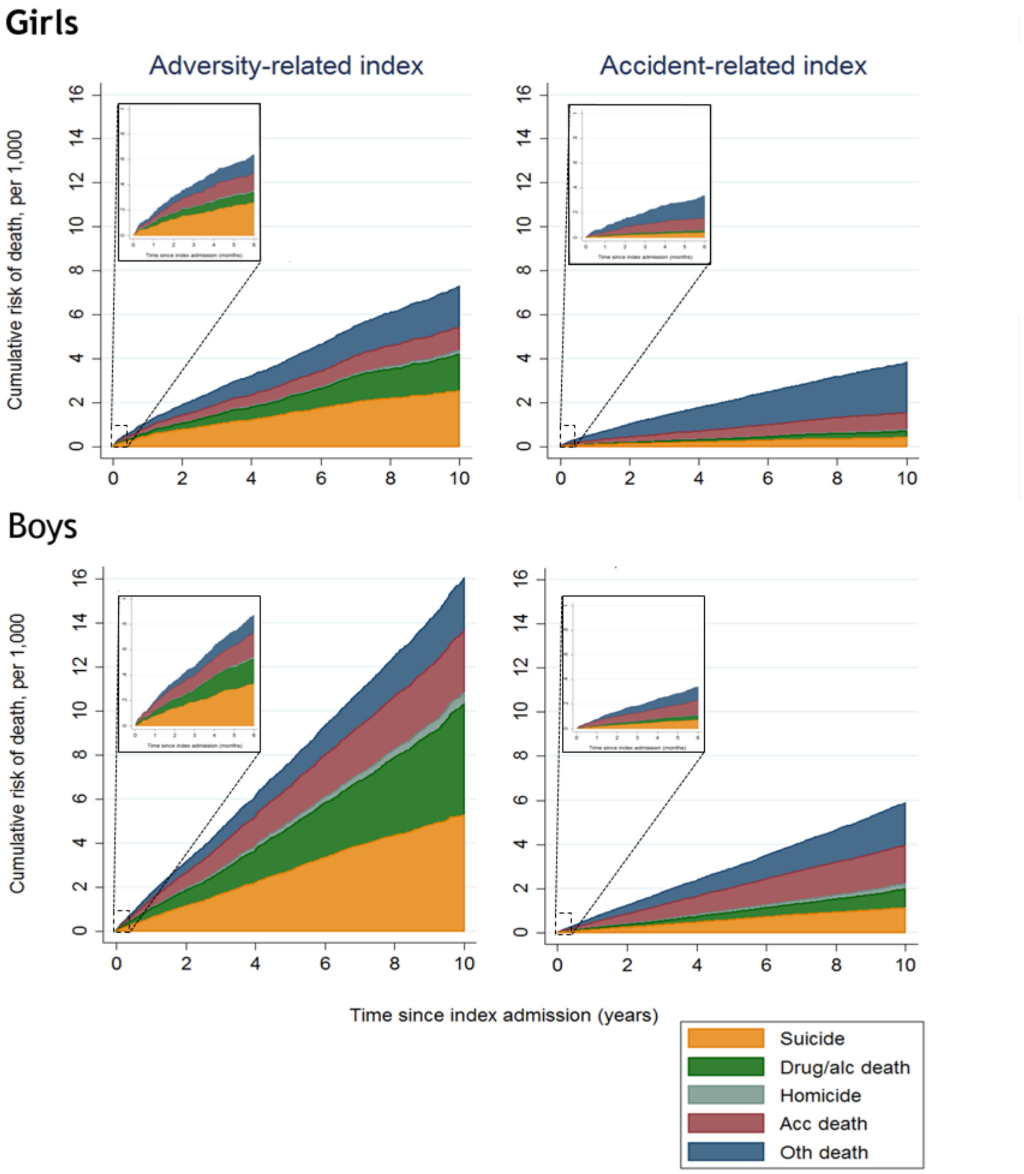
		Numbers of deaths by cause (row %)											
Sex **Type of injury at index admission**	**Discharged**	**Total**		**Adversity-related***		**Suicide**		**DA**		**Accidental**		**Other**	
Girls	348 388	1 312	(100.0)	603	(46.0)	361	(27.5)	319	(24.3)	228	(17.4)	481	(36.7)
Accident-related	166 462	439	(100.0)	85	(19.4)	47	(10.7)	41	(9.3)	94	(21.4)	260	(59.2)
Adversity-related	181 926	873	(100.0)	518	(59.3)	314	(36.0)	278	(31.8)	134	(15.3)	221	(25.3)
Self-inflicted	131 739	651	(100.0)	408	(62.7)	259	(39.8)	210	(32.3)	93	(14.3)	150	(23.0)
DA	163 888	776	(100.0)	464	(59.8)	283	(36.5)	250	(32.2)	117	(15.1)	195	(25.1)
Violent	13 262	54	(100.0)	25	(46.3)	10	(18.5)	16	(29.6)	11	(20.4)	18	(33.3)
Boys	634 439	3 470	(100.0)	1 736	(50.0)	903	(26.0)	861	(24.8)	891	(25.7)	843	(24.3)
Accident-related	483 356	1 928	(100.0)	711	(36.9)	375	(19.5)	311	(16.1)	600	(31.1)	617	(32.0)
Adversity-related	151 083	1 542	(100.0)	1 025	(66.5)	528	(34.2)	550	(35.7)	291	(18.9)	226	(14.7)
Self-inflicted	44 621	704	(100.0)	526	(74.7)	304	(43.2)	276	(39.2)	92	(13.1)	86	(12.2)
Violent	70 594	460	(100.0)	268	(58.0)	120	(26.1)	135	(29.2)	122	(26.4)	70	(15.2)
DA	85 421	1 112	(100.0)	775	(69.5)	418	(37.6)	424	(38.1)	183	(16.5)	154	(13.8)

DA = Drug/alcohol-related
*Suicides, homicides and drug/alcohol-related deaths. These deaths were not mutually exclusive. Explicit numbers and proportions are not reported for homicides due to small counts.

7.4.1 Objective 5: Risks of cause-specific deaths following adversity-related and accident-related injury

Most deaths which occurred following adversity-related injury were also adversity-related (girls 59.3%, boys 66.5%; Table 7.1), of which most were suicides (girls 35.8% of all deaths, boys 34.2%) or drug/alcohol-related (girls 31.7%, boys 35.6%). For adolescents who died following accident-related injury, most deaths were accidental (girls 21.4%, boys 31.3%) or through other causes (girls 60.8%, boys 32.2%).

Cumulative risks of death were approximately two to three times higher following adversity-related injury than following accident-related injury at all time-points in the ten years post-discharge (girls with adversity-related injury: 7.3/1,000 by 10y, 95% CI: 6.8 to 7.8, accident-related injury: 3.7/1,000, 3.4 to 4.1; boys with adversity-related injury: 15.6/1,000, 14.8 to 16.4, accident-related injury: 6.0/1,000, 5.7 to 6.3) (Figure 7.2; Appendix H.1) (256). These differences were principally driven by differences in risks of suicide and drug/alcohol-related deaths, which were substantially higher at all time-points after adversity-related injury (Figure 7.2).

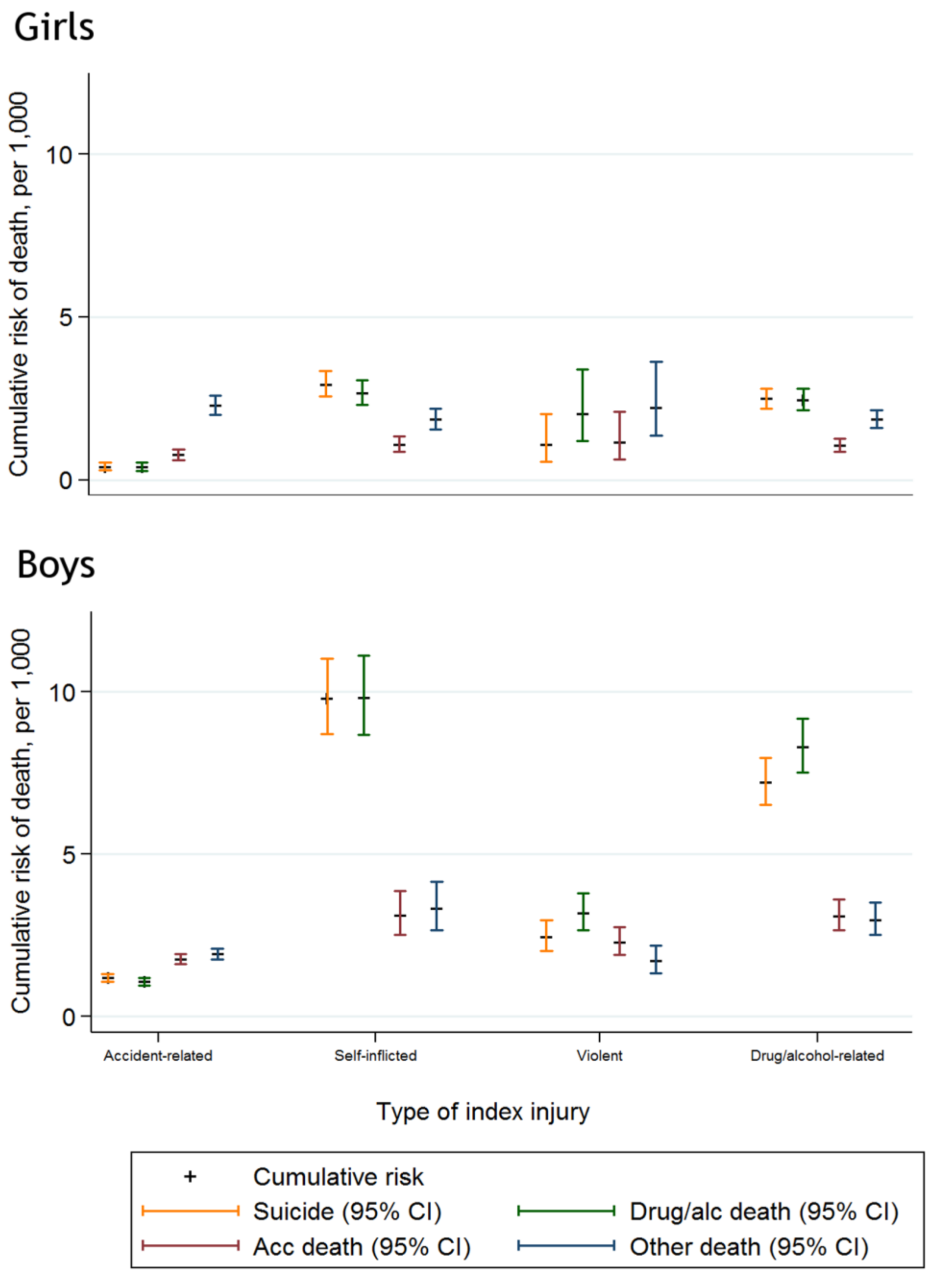


Drug/alc = Drug/alcohol-related; Acc = Accidental; Oth = Other; 'Suicide' includes all suicide deaths, whether homicide or drug/alcohol-related death were also implicated or not; Drug/alc death includes only drug/alcohol-related deaths where suicide was not also implicated; 'Homicide' includes only where suicide or drug/alcohol-related death was not also implicated.

Figure 7.2. Cumulative risks of cause-specific death over time, by sex and adversity-related or accident-related injury at index admission

Risks after violent, self-inflicted, and drug/alcohol-related injury

By ten years post-discharge, risks of suicide and drug/alcohol-related deaths were all higher following adversity-related injury compared to accident-related injury, regardless of whether the original injury was violent, self-inflicted, or drug/alcohol-related (Figure 7.3). In addition, these risks of suicide and drug/alcohol-related death were similar. For example, after self-inflicted injury, the 10y risk of suicide for girls was 2.9/1 000 (95% CI: 2.6 to 3.3), whereas the 10y risk of drug/alcohol-related death was 2.7/1 000 (2.3 to 3.1) (Figure 7.3; Appendix H.1). Risks of accidental and other deaths were higher following self-inflicted and drug/alcohol-related injury (compared to accident-related injury), in boys but not girls.



Drug/alc = Drug/alcohol-related; Acc = Accidental; Oth = Other;

Figure 7.3. 10y cumulative risks of cause-specific deaths, by sex and type of injury at index admission

Similar patterns were observed when risks were stratified by age-group (Appendix H.1). Older boys were at particularly high risks of all-cause death after self-inflicted injury (10y risk: 30.4/1 000, 95% CI: 27.4 to 33.7; or 1 per 33 boys). This was driven by remarkably high risks of suicide (11.8/1 000, 10.4 to 13.8; 1 per 85) and drug/alcohol-related deaths (14.0/1 000, 12.0 to 16.4; 1 per 71).

Relative risks adjusted for other covariates

Risks of suicide and drug/alcohol-related deaths after adversity-related injury were three to five times higher than after accident-related injury, after adjusting for differences in age and prevalence of chronic conditions (adjusted SHR for suicide, girls: 4.52, 95% CI: 3.24 to 6.30, boys: 3.28, 2.85 to 3.78, adjusted SHR for drug/alcohol-related death, girls: 4.93, 3.45 to 7.04, boys: 3.78, 3.26 to 4.37; Table 7.2). Boys admitted with adversity-related injury also had significantly higher risks of accidental death (adjusted SHR: 1.29, 95% CI: 1.11 to 1.50), but not girls (1.20, 0.89 to 1.62).

Among adolescents admitted with either adversity-related or accident-related injury, there was an independent two-fold increased risk of death post-discharge for those older at their index admission (e.g., 18-19y vs. 10-14y), accounted for by increased risks of suicide, homicide, drug/alcohol-related, and accidental deaths (adjusted SHRs ranged from 1.13 to 5.01, by sex, age-group and cause of death; Table 7.2). There was a three- to four-fold independently increased risk of death for those with a chronic condition (vs. none), principally due to an increased risk of deaths through other causes (girls, adjusted SHR: 10.28, 95% CI: 8.40 to 12.58, boys: 11.85, 10.21 to 13.75).

Table 7.2. Adjusted relative risks of cause-specific death after adversity-related injury (versus accident-related injury), by sex

	Cause of death, Sub-hazard ratio (95% Confidence Interval)									
Sex **Characteristic at index admission**	**All deaths**		**Suicide**		**DA death**		**Accidental death**		**Other death**	
Girls										
Adversity- (vs. accident-related) injury	1.51	(1.34 to 1.71)	4.52	(3.24 to 6.30)	4.93	(3.45 to 7.04)	1.20	(0.89 to 1.62)	0.66	(0.55 to 0.79)
Age-group (vs. 10-15y)										
16-17y	1.40	(1.21 to 1.61)	2.30	(1.63 to 3.24)	1.87	(1.35 to 2.61)	1.13	(0.80 to 1.58)	1.07	(0.86 to 1.34)
18-19y	2.10	(1.82 to 2.42)	4.30	(3.08 to 6.02)	2.76	(1.98 to 3.86)	1.59	(1.12 to 2.25)	1.44	(1.16 to 1.79)
Chronic condition (vs. none)	3.77	(3.38 to 4.20)	1.92	(1.55 to 2.37)	2.55	(2.04 to 3.18)	2.36	(1.82 to 3.09)	10.28	(8.40 to 12.58)
Boys										
Adversity- (vs. accident-related) injury	2.02	(1.88 to 2.17)	3.28	(2.85 to 3.78)	3.78	(3.26 to 4.37)	1.29	(1.11 to 1.50)	1.01	(0.86 to 1.19)
Age-group (vs. 10-15y)										
16-17y	1.72	(1.57 to 1.88)	2.68	(2.19 to 3.28)	3.03	(2.40 to 3.81)	1.59	(1.35 to 1.88)	1.14	(0.97 to 1.34)
18-19y	2.22	(2.03 to 2.43)	3.45	(2.81 to 4.23)	5.01	(4.00 to 6.27)	1.90	(1.60 to 2.26)	1.21	(1.02 to 1.44)
Chronic condition (vs. none)	2.66	(2.49 to 2.85)	1.28	(1.09 to 1.50)	1.83	(1.58 to 2.12)	1.63	(1.41 to 1.90)	11.85	(10.21 to 13.75)

Each column (by sex) represents a separate Fine & Gray's competing risks model. Adversity (vs. accident-related) injury, age-group and chronic condition (vs. none) were entered as independent variables simultaneously, per model.
DA = Drug/alcohol-related

Model checks

Tests for non-zero slope of Schoenfeld residuals, and a time-varying covariate for adversity-related (vs. accident-related) injury, did not indicate a violation of the assumption that sub-distribution hazards were proportional across models (for girls, boys, and different causes of death as the outcome of interest). The link-test indicated that the competing risks models adequately fitted the data.

7.5 Discussion

This study showed that the findings of Study III, that is, that there are increased risks of death after adversity-related injury compared to after accident-related injury, is accounted for by the increased risks of suicide and drug/alcohol-related deaths (and additionally in the case of boys, accidental deaths). This was the case for all three types of adversity-related injury. In addition, for each type of adversity-related injury, risks of drug/alcohol-related deaths were just as high as those for suicide. This latter finding has implications for hospital management of adolescents, where risks of suicide death are treated as a priority.

7.5.1 Strengths and limitations

To my knowledge, this study is the largest and most recent to follow adolescents following an admission for self-inflicted injury (see results of systematic review in Section 1.5.3), and the only study to quantify cause-specific risks of death following violent or drug/alcohol-related injury. Linked mortality data containing the underlying and up to 15 contributing causes of death allowed me to capture all deaths occurring in the ten years after discharge and all attributed causes.

I have previously discussed the limitations of relying on ICD-10 codes in HES to define adversity-related and accident-related injury (Section 6.5.1). There are similar drawbacks to relying on ICD-9 and -10 codes to classify causes of deaths. That is, adversity-related deaths are likely to be under-recorded, and may be misclassified as accidental or other causes of death. This misclassifcation would lead to under-estimation of risks of adversity-related deaths. Therefore, in reality, adversity-related deaths may contribute a higher burden of deaths in adolescents admitted with adversity-related injury than the approximate 70% found in this study. However, we can be confident that this under-estimation has not driven the finding of similar risks of suicides and drug/alcohol-related deaths after all types of injury. These risks were similar even when deaths labelled as 'undetermined intent' were classified as suicides.

7.5.2 Comparisons with other studies

The distribution of causes of deaths in our study was comparable to Hawton *et al*'s cohort study of 15-24y olds presenting to hospital with self-inflicted injury (82). The authors reported risks of death up to 20y later of 29/1 000, of which 48% were from suicide (including deaths of undetermined intent) and 21.4% were accidental. In our study, for adolescents admitted with self-inflicted injury the risks of death post-discharge were 7.7/1 000 for girls and 24.1/1 000 for boys (Appendix G.4), of which 39.8% and 43.2% were for suicide, and 14.3% and 13.2% were accidental (Table 7.1). Our proportions of suicides and accidental are likely to be slightly lower than Hawton *et* al's because of the difference in age-ranges between the two studies (Hawton *et al*: deaths captured at 15-44y old, current study: 10-29y old), and categorisation of accidental deaths (Hawton *et al* included drug/alcohol-related deaths in their definition, whereas I did not).

To my knowledge there are no other reports of risks of cause-specific death after violent injury or drug/alcohol-related injury during adolescence, or official rates of homicide, drug/alcohol-related, or accidental deaths by age, with which to compare our findings.

7.5.3 Implications of findings

Research in adult self-harm patients has revealed increased risks of alcohol-related harms (56, 262), but until now the relationship between one type of adversity-related injury and risks of future harm through other types of adversity had not been confirmed for adolescents. The finding that girls and boys admitted with any type of adversity-related injury are at increased risks of suicide and drug/alcohol-related deaths (and that boys are at increased risks of accidental deaths), further justify development of clinical guidelines for violent and drug/alcohol-related injury to address the psychosocial needs of adolescents (Table 1.3). However more importantly, these findings advocate for a shift in public health prevention to not only focus on reducing risks of suicide death in this group, but also risks of drug/alcohol-related death. Suicide and drug/alcohol-related deaths contributed similar burdens in risks and total numbers of deaths in the ten years after discharge.

Although I analysed data for the entire population of interest, numbers of homicide were small (counts in most groups being lower than five). Therefore, I could not present some of these numbers or estimated risks of homicide. Reliable estimates of the risks of homicide following adversity-related injury during adolescence may only be possible through international collaborations of large datasets, similar to that of the Child & Adolescent Self-harm in Europe (or 'CASE') (263), or the European School Survey project on Alcohol and other Drugs (or 'ESPAD) studies (213).

Chapter 8 Synthesis of thesis findings

8.1 Chapter summary

This chapter brings together the findings of Chapters 1 to 7, and discusses what these findings contribute to policy, practice, and future research.

In Section 8.3, I briefly discuss what was previously known about adolescents with adversity in England. I then summarise the main findings of the three research studies in this thesis.

I follow in Section 8.4 by discussing the main limitations overall of this thesis. I describe ways in which this research could be taken forward to overcome these limitations. For example, there were no official clusters of codes available for drug/alcohol misuse. Such a cluster could be developed by cross-referencing with medical notes, and in collaboration with clinicians, to improve detection of this activity among adolescents in hospital data.

Next, in Section 8.5 I discuss the main implications of the findings of this thesis for policymakers and NHS service planning. For example, national clinical guidelines that recommend psychosocial assessment in adolescents presenting with self-inflicted injury should extend these recommendations to other types of adversity-related injury, where risks of future harm are just as high. I discuss the implications that such recommendations would have for service planning.

I conclude this thesis with the recommendation that guidelines, training, information sharing, and interventions be developed, towards reducing the risks of future harm for adolescents hospitalised with adversity-related injury.

8.2 Introduction

In Chapters 1 to 7, I described: reviews of the literature regarding adolescents with adversity and the known burden of morbidity and mortality in this group, and data sources, statistical methods, results, and conclusions of three research studies used to characterise the population of adolescents who are admitted to hospital as an emergency for adversity-related injury and estimate their risks of future harm. Here, the findings in Chapters 1 to 7 are discussed as a whole, and I set out the wider implications for policy, practice and research.

8.3 What this thesis adds to the literature

It was already known that (Chapter 1):

- up to 70% of individuals in the general population in England are exposed to adversity (violence, self-harm, or drug/alcohol-misuse) during their adolescence
- adversity accounts for the most common causes of mortality and morbidity among adolescents
- adversity during adolescence is associated with increased risks of harm and suffering through to as late as mid-adulthood (around 50 years old).

Very little was known about the sub-population of adolescents who are hospitalised with adversity-related injury, a population with the propensity to benefit from interventions to reduce harm.

In this thesis, I described the prevalence, socio-demographic and clinical characteristics of adolescents admitted with adversity-related injury (violent, drug/alcohol-related, or self-inflicted injury), and their long-term risks of future harm. Principal findings were that:

- The prevalence of an emergency admission for adversity-related injury was approximately 1 in every 25 for adolescents, this prevalence being similar for girls and boys.
- Adolescents admitted as an emergency with adversity-related injury were most likely to be older (18-19 years old), and resident of relatively deprived areas.
- Among adolescents admitted as an emergency with adversity-related injury, approximately three-quarters of girls and one-third of boys were admitted with more than one type of adversity-related injury (i.e., violent, self-inflicted, or drug/alcohol-related) between 10 and 19 years old. There was a large overlap between self-inflicted and drug/alcohol-related injury.
- The risks of death in the ten years following adversity-related injury were 1 in every 137 for girls, and 1 in every 64 for boys; the risks of emergency re-admission were 54.2% for girls and 40.5% of boys.
- Risks of death and emergency re-admission in the ten years following adversity-related injury were approximately twice the risks following accident-related injury. These risks were similarly increased after all types of adversity-related injury.
- The increased risks of death following an emergency admission for adversity-related injury during adolescence (vs. accident-related injury) were mainly accounted for by increased risks of suicides and drug/alcohol-related deaths.
- Risks of drug/alcohol-related deaths were as high as those for suicide deaths, after each type of adversity-related injury.

The findings of this thesis are most relevant for development of policies and service planning in NHS hospitals around management of adolescents with adversity-related injury. The estimated prevalence and risks of death and emergency re-admission may be generalised to other hospitalised adolescent populations within the UK and other parts of Europe, where patterns of self-harm and drug/alcohol use during adolescence have been shown to be similar (213, 263).

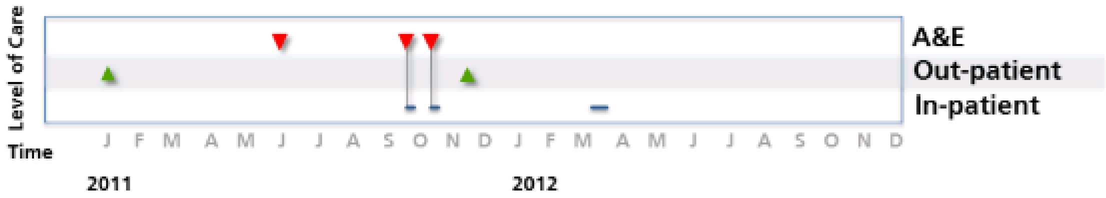
8.4 Limitations of this thesis and further research

The interpretation of findings in this thesis rest heavily on assumptions about the sensitivity of ICD-10 codes for capturing adversity-related injury, and about the level of false and missed matches within HES and between HES and ONS data. These assumptions indicate how underestimated the prevalence of adversity-related injury, risks of future harm, or the difference in risks following adversity-related and accident-related injury, may be.

It is currently unclear how variable the diagnosis of self-harm with undetermined intent is, and there are no validated clusters of codes available for drug or alcohol misuse. Further work could elucidate the validity of ICD-10 codes for capturing different types of adversity-related injury and whether this validity varies for different sub-groups (e.g., by sex). This work could include validating self-harm and drug/alcohol use codes against medical records, or with a panel of clinicians and NHS coders, as done for victimisation and chronic conditions (154, 166, 180, 198). These clusters need to be developed particularly for children and young people, where presentations would substantially differ, compared to adults.

Analyses of administrative data, even with validated clusters of codes for adversity, will not capture some of the nuances of a clinician-patient consultation. Administrative data provide crude estimates of the risks of future harm for the whole population of adolescents who are admitted with adversity-related injury, and indications of who may benefit from intervention. Qualitative research in some of these adolescents and the clinicians who treat them could provide more insight into the variation of these risks of future harm.

Younger adolescents in the study cohorts of this thesis (i.e., 10-15 year olds) were likely to highly represent adolescents who present to the emergency department with self-inflicted injury, as NICE guidelines mandate admission for presentation of self-harm in under 16 year olds (58). However, we do not know if patterns found in our cohort would be similar for older adolescents who present to the emergency department but are not necessarily admitted, or those who have adversity-related injury recorded at outpatient visits. Figure 8.1 illustrates the encounters that an adolescent may have with hospital services, that HES inpatient data alone would not capture. Following the findings in this thesis according to admitted adolescents, similar work in these other populations would be justified, and more feasible in the coming years as administrative datasets for ED and outpatient visits improve (141). Linkage to other healthcare data (e.g., GP or CAMHS) or non-healthcare data (e.g., social services, schools) could give an improved indication of mental health conditions (for both the adolescent and their immediate family, e.g., parental alcohol issues) (166), and an understanding of where recognition and treatment of adversity is currently already occurring or lacking.



Taken from presentation at the Royal Statistical Society in 2014[6].

Figure 8.1: Hypothetical example of a patient's different hospital contacts over time

8.5 Implications for policy and practice

The burden of admissions for adversity-related injury during adolescence was substantial. Adolescents admitted with adversity-related injury accounted for at least 140,000 of 10-19 year olds in 1997-2011 (Table 4.6). They represented twice as much burden of numbers of admissions as adolescents with chronic conditions (adolescents admitted with injury not related to adversity or accidents, comprising principally of adolescents with chronic conditions; Table 4.6). Both measures to prevent adversity-related injury during adolescence, and to improve management during these admissions for adversity-related injury, have the potential to reduce the risk of adverse outcomes later in the life-course, and to relieve burden on public, particularly hospital, services.

Public health initiatives to reduce risk-taking behaviours could result in fewer admissions for adversity-related injury and the associated subsequent harms (215). We recently compared time-trends of admissions of adolescents for adversity-related injury from 2005 and 2011, between England and Scotland. There was a steeper decreasing trend in incidence in Scotland, particularly for older adolescents. The study concluded that some of these differential trends between the two countries could likely be attributed to the different approaches to reducing child maltreatment and neglect, gang activity, under-age drinking, parental drug use, and mental health issues among young people.

Policymakers could consider how we may capitalise on this moment of admission for adversity-related injury to reduce risks of future harm for these individuals. National clinical guidelines should be developed or modified (Table 1.3), to reflect the fact that whichever type of adversity-related injury the adolescent presents with, this is likely to signal vulnerability and increased risks of future harm. Developments could include extending mandated psychosocial assessment from self-inflicted injury to all three types of adversity-related injury. Adolescents admitted with self-inflicted and drug/alcohol-related injury, who are male, older, from deprived areas, or have a chronic condition, and where the burden of numbers of admissions and risks of future harm is particularly high, should be flagged as a particularly vulnerable group for future harm. Drug/alcohol-related deaths need to be prioritised as a concern, as they were shown to be just as likely as suicide deaths in the ten years after discharge from any adversity-related injury.

Consideration of psychological and social circumstances is good clinical practice, particularly for vulnerable adolescents, who will represent the approximately one-third of those admitted with injury (Section 4.4.1). However, extending mandated psychosocial assessment from self-inflicted injury to all three types of adversity-related injury may have implications for services. Injured young people aged 16 years or older are often managed on adult surgical wards in the NHS, where expertise in psychosocial assessment and support for young people may be limited (47). Relevant training of health professionals on these wards could be written into individual service protocols.

This may go some of the way to improving rates of psychosocial assessment in general, that are currently estimated to be around 50-60% for patients presenting with self-inflicted injury (47, 264). Training may additionally improve overall experiences and engagement for the adolescents who do receive assessment (47, 265), that have already been highlighted as issues for delivering effective intervention.

Currently, clinicians are not guaranteed to have easy access to hospital or GP records for the adolescent in front of them, to know whether he/she has a previous history of mental health problems, is often admitted with injury, or has had a previous psychosocial assessment. Improved access to medical records could increase the ability for the clinician to deliver appropriate assessment and management plans at discharge. In this thesis, some of the highest risk groups were characterised by adversity and healthcare contacts across a number of admissions. For the relatively small number of adolescents exposed to all three types of adversity-related injury (n=1,485 girls and 1,657 boys; Appendix E.1), only 33.9% of girls and 20.0% of boys had all three types recorded at the same admission. These are likely to be some of the most complex cases of psychosocial need, supported by the fact that in this thesis, this sub-group of adolescents had the highest proportion to be admitted three or more times (Table 4.7, Table 4.8), and were at the highest risks of death or emergency re-admission within the next ten years (Figure 6.7, Figure 6.8).

Though it is clear that adolescents with adversity-related injury are at increased risks of future harm, the systematic review in Chapter 1 (Section 1.6) revealed that the optimal ways to manage these adolescents to reduce such harm remain unclear. There needs to be more investment in finding effective interventions for reducing harm following adversity-related injury, particularly following violent or drug/alcohol-related injury, for which large UK-based trials in adolescent groups are scarce (98, 100, 266).The findings of this thesis advocate measuring broader outcomes, and in the case of death at least, following adolescents beyond the standard 1-2 years currently done in relevant trials (Table 1.5; in this thesis, risks consistently increased in the ten years after discharge; Figure 6.3). Linkage to administrative data could circumvent some of the financial and labour costs associated with trials of long-term follow-up. Further qualitative research in adolescents presenting or admitted with adversity-related injury may shed light as to the mechanisms (e.g., youth worker, mental health, or social support), that need to be included in interventions, as well as barriers to successful delivery and effectiveness (267).

8.6 Concluding remarks

The findings in this thesis should inform the development of clinical guidelines and service planning. There should exist guidelines for managing adolescents with violent and drug/alcohol-related injury to reduce their risks of future harm, that consider underlying psychosocial need to the same level as guidelines for managing those with self-inflicted injury. This should be coupled with appropriate training of staff, development of effective interventions and increased information sharing, such that recommendations can be optimised.

Appendices

A. Systematic review of studies reporting risks of harm following an admission for adversity-related injury

A.1 Search terms

(“adolescen*” OR “child*” OR “young” OR “youth” OR “juvenile” OR “teen*”)[Title/abstract] with (“injur*” AND (“hospital” OR “hospitali*” OR “admission” OR “admitted” OR “emergency”) [Title/abstract]) with (“victim*” OR “assault” or “maltreat*” OR “violence” OR “abuse*” OR “self-harm” OR “suicid*” OR “self-inj* OR “substance*” OR “drug*” OR “cannabis” OR “marijuana” OR “opiate*” OR “opioid*” OR “ecstasy” OR “solvent*” OR “cocaine” OR “addict*” OR “alcohol” OR “drink” OR “drunk” OR “intoxicat*” OR “narcotic*” OR “amphetamine*”)[Title/abstract] AND ("1995/01/01"[Date - Publication] : "2015/01/31"[Date - Publication])

A.2 The Quality in Prognostic Studies (QUIPs) tool (70), modified for current systematic review

Domains	Items for consideration	Ratings
Study participation	a. Adequate participation in the study by eligible persons b. Description of the source population or population of interest c. Description of the baseline study sample d. Adequate description of the sampling frame and recruitment e. Adequate description of the period and place of recruitment f. Adequate description of inclusion and exclusion criteria	**High bias:** The relationship between the PF and outcome is very likely to be different for participants and eligible nonparticipants **Medium bias:** The relationship between the PF and outcome may be different for participants and eligible nonparticipants **Low bias:** The relationship between the PF and outcome is unlikely to be different for participants and eligible nonparticipants
Study attrition	a. Adequate response rate for study participants b. Description of attempts to collect information on participants who dropped out. c. Reasons for loss to follow-up are provided. d. Adequate description of participants lost to follow-up. e. There are no important differences between participants who completed the study and those who did not	**High bias:** The relationship between the PF and outcome is very likely to be different for completing and non-completing participants **Moderate bias:** The relationship between the PF and outcome may be different for completing and non-completing participants **Low bias:** The relationship between the PF and outcome is unlikely to be different for completing and non-completing participants
Prognostic factor measurement*	a. Definition of the PF b. Valid and reliable measure of PF c. Method and setting of PF measurement ~~d. Proportion of data on PF available for analysis~~ e. ~~Method used for missing data~~	**High bias:** The measurement of the PF is very likely to be different for different levels of the outcome of interest **Moderate bias:** The measurement of the PF may be different for different levels of the outcome of interest **Low bias:** The measurement of the PF is unlikely to be different for different levels of the outcome of interest
Outcome	a. A clear definition of the outcome is provided	**High bias:** ~~The measurement of the outcome is very likely to be~~

measurement	b. Method of outcome measurement used is adequately valid and reliable c. The method and setting of outcome measurement is the same for all study participants.	~~different related to the baseline level of the PF~~ The absolute risk of outcome following the PF is likely to be under/over-estimated **Moderate bias:** ~~The measurement of the outcome may be different related to the baseline level of the PF~~ The absolute risk of outcome following the PF may be under/over-estimated **Low bias:** ~~The measurement of the outcome is unlikely to be different related to the baseline level of the PF~~ The absolute risk of outcome following the PF is unlikely to be under/over-estimated
~~Study confounding~~**	~~a. All important confounders are measured~~ ~~b. Clear definitions of the important confounders measured are provided~~ ~~c. Measurement of all important confounders is adequately valid and reliable~~ ~~d. The method and setting of confounding measurement are the same for all study participants~~ ~~e. Appropriate methods are used if imputation is used for missing confounder data~~ ~~f. Important potential confounders are accounted for in the study design~~ ~~g. Important potential confounders are accounted for in the analysis.~~	~~**High bias:** The observed effect of the PF on the outcome is very likely to be distorted by another factor related to PF and outcome~~ ~~**Moderate bias:** The observed effect of the PF on outcome may be distorted by another factor related to PF and outcome~~ ~~**Low bias:** The observed effect of the PF on outcome is unlikely to be distorted by another factor related to PF and outcome~~
Statistical analysis and reporting***	~~a. Sufficient presentation of data to assess the adequacy of the analytic strategy~~ ~~b. Strategy for model building is appropriate and is based on a conceptual framework or model~~ ~~c. The selected statistical model is adequate for the design of the study~~ d. There is no selective reporting of results *e. Analyses take drop-out over time into account* f. *Results are reported with confidence intervals, or at least numbers and proportions can be used to estimate confidence intervals post-report.*	**High bias:** The reported results are very likely to be spurious or biased related to analysis or reporting **Moderate bias:** The reported results may be spurious or biased related to analysis or reporting **Low bias:** The reported results are unlikely to be spurious or biased related to analysis or reporting

PF = Prognostic Factor

Reproduced from Hayden *et al*, Ann Intern Med, 2013 (70), with modifications indicated. Items from the original QUIPS tool that have been removed for the current review have been ~~struck through~~. Items that have been added to the original QUIPs tool are presented in *italics*.

*Items d. and e. were removed because the PF (i.e., violence, self-harm or drug/alcohol misuse) could not feasibly be missing in this review.

**Items a.-g. were removed because the objective of the review was to quantify the 'natural' absolute risks of harm, regardless of confounding.

***Item a. was removed because presenting at least absolute proportions with outcomes following discharge was one of the inclusion criteria in the current review, and so there could be little variation in how data was presented. Items b.-c. were removed because confounding was not of interest in the current review, and therefore so were models to adjust for it. Item e. was added because drop-out could affect whether absolute risks were under- or over-estimated. Item f. was added because confidence intervals could be used to assess how precise estimated risks were likely to be.

A.3 Articles that could not be retrieved through the University College London Library Service

1. Randall B, Wilson A, Regional I, Child Mortality Review C. The 2008 annual report of the Regional Infant and Child Mortality Review Committee. South Dakota medicine: the journal of the South Dakota State Medical Association. 2009;62(12):471-3, 5-7.

2. McAnally HM, Kypri K. Alcohol and road safety behaviour among New Zealand tertiary students. International journal of adolescent medicine and health. 2004;16(3):229-37.

3. Foley DS, Draus JM, Jr., Santos AP, Franklin GA. An analysis of risk-taking behavior among adolescent blunt trauma patients. The Journal of the Kentucky Medical Association. 2009;107(5):170-5.

4. van As AB, Withers M, du Toit N, Millar AJ, Rode H. Child rape--patterns of injury, management and outcome. South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde. 2001;91(12):1035-8.

5. Greene D, Raven R, Carvalho G, Maas CS. Epidemiology of facial injury in blunt assault. Determinants of incidence and outcome in 802 patients. Archives of otolaryngology--head & neck surgery. 1997;123(9):923-8.

6. Kupferschmid S, Gysin-Maillart A, Buhler SK, Steffen T, Michel K, Schimmelmann BG, et al. Gender differences in methods of suicide attempts and prevalence of previous suicide attempts. Zeitschrift fur Kinder- und Jugendpsychiatrie und Psychotherapie. 2013;41(6):401-5.

7. Greenblatt JF, Dannenberg AL, Johnson CJ. Incidence of hospitalized injuries among pregnant women in Maryland, 1979-1990. American journal of preventive medicine. 1997;13(5):374-9.

8. Velmahos GC, Safaoui M, Demetriades D. Management of shotgun wounds: do we need classification systems? International surgery. 1999;84(2):99-104.

9. Congeni J. Management of the adolescent concussion victim. Adolescent medicine: state of the art reviews. 2009;20(1):41-56, viii.

10. Phang I, Mathieson C, Sexton I, Forsyth S, Brown J, St George EJ. Paediatric head injury admissions over a 10-year period in a regional neurosurgical unit. Scottish medical journal. 2012;57(3):152-6.

11. Flannery RB, Jr., Hanson MA, Corrigan M, Walker AP. Past violence, substance use, and precipitants to psychiatric patient assaults: eleven-year analysis of the Assaulted Staff Action Program (ASAP). International journal of emergency mental health. 2006;8(3):157-63.

A.4 Risks of future harm, reported by articles included in systematic review

Type of adversity Lead author, year	**Follow-up**	**N**	**Risks of future harm**
Violence			
Downey 2007 (84)	1 month, follow-up survey by telephone	84	11 violence-related outcomes, from 2%* who threatened someone with a knife/gun in the past month, to 40% having pushed or shoved someone 10% needed medical attention
Wiebe 2011 (87)	1 to 8 weeks by interactive voice-response survey (accessible by a toll-free number which was provided to patients)	42	30.9% were threatened 18.1% threatened someone 18.2% were beaten up 20.7% had beaten up someone 2.9% were shot or stabbed or shot or stabbed someone 12.9% sustained an injury that required medical attention by 4 weeks 38.1% were threatened 21.5% had threatened someone 18.2% were beaten up 20.7% had beaten up someone 2.9% were shot or stabbed or shot or stabbed someone 12.9% sustained an injury that required medical attention by 8 weeks
Cassidy 2009 (75)	1-6 years, by telephone survey	39	25.8% (8/31) girls and 0% boys stated (or their parents stated) that they had repeat self-harmed 50.0% (4/8) of girls who repeat self-harmed did so more than once

Type of adversity Lead author, year	Follow-up	N	Risks of future harm
Self-inflicted injury			
Cotgrove 1995 (85)	1 year, by gathering information from clinic and hospital notes and contacting other involved professionals by letter, e.g. GP	58	12.1% made a repeat suicide attempt
Goldston 1999[†] (73)	5 years, by face-to-face interviews and self-report questionnaires	75	~17%** who had 1 previous suicide attempt before hospitalisation repeated an attempt ~36% who had >1 previous suicide attempt before hospitalisation repeated an attempt 0 completed suicide
Granboulan 1995 (77)	7-17 years (mean 11.5 years), by self-report questionnaire, face-to-face interview (if consented) and telephone contact with patient, family member or physician (if did not consent to face-to-face interview)	127	30.7% made at least one further suicide attempt 11.8% died in total: 3.9% (5/127) through suicide, 7.1% (9/127) of unnatural or violent causes other than suicide, e.g. substance abuse, and 0.8% (1/127) of epilepsy
Groholt 2006 & 2009 (78, 81)	7.5-10.5 years (mean 9 years), by interview For the 5 that had died, parents were interviewed or medical authorities contacted	92	~35.0% (Kaplan-Meier estimate) made at least one further suicide attempt (highest risk within two weeks) 10% made four or more further suicide attempts 5.7% died in total: 2.2% (2/92) by suicide, 2.2% (2/92) by accidental overdose and 1.1% (1/92) by a somatic disorder
Harrington 1998 (88)	6 months, by self-report questionnaire	77	14.7% repeat self-harmed
Hawton 1999 (89)	1 year, by Oxford Monitoring system for attempted suicide	45	20.0% re-presented with self- poisoning or injury to a hospital in Oxford
Hawton 2007 (82)	1 day to 23 years (median 11 years), death certificate information traced through Office for National Statistics for England and Wales and General Register Office in Scotland	2,839 15-19y olds	1.4% attempted suicide
Hawton 2012 (90)	2-7 years (average follow-up not reported), by hospital data for re-presentations	3,920	27.3% re-presented with self-harm

Type of adversity Lead author and year	Follow-up	N	Outcomes/summary of findings
Self-inflicted injury (continued)			
Hawton 2012 (90)	3-11 years (average follow-up not reported), by Medical Research Information Services of the NHS (flagged by Central Health Registry Inquiry System)	5,205	0.8% died in total: 0.2% (15/51) by suicide, 0.2% (10/51) undetermined, 0.2% (13/51) accidental and 0.2% (13/51) other
Hulten 2001 (76)	0-7 years (mean 3.9 years), by monitoring any contacts with healthcare	1,215***	16.2% (148/915) girls and 18.1% (63/349) boys made at least one further suicide attempt
Laurent 1998 (79)	1-11 years (mean 5.3 years), by departmental registers.	552	17.4% made at least one further suicide attempt 1.8% died in total: 0.9% (5/552) through suicide, 0.2% (1/552) from an aggressive attack, and 0.7% (4/552) for unknown reasons
Rotheram-Borus 2000 (80)	1.5 years, by face-to-face interviews and monitoring of admissions data.	75	14.7% made at least one further suicide attempt
Violence and drug/alcohol misuse			
Cunningham 2015 (91)	24 months, by ED medical records and self-report data from surveys at 6, 12, 18 and 24 months. Authors reported cumulative outcomes at 24 months only.	599	37.0% (129/349) presenting with violent and drug-related injury returned to the ED for a violent injury 22.4% (56/250) presenting with drug-related injury only returned for a violent injury 0.8% (5/559) died in total: died in total: 0.5% (3/559) from an aggressive attack, 0.2% (1/559) through a drug overdose and 0.2% (1/559) from a road traffic accident at 24 months

Violence and drug/alcohol misuse (continued)			
Walton 2010 & Cunningham 2012 (55, 86)	3, 6, and 12 months, by face-to-face interview	235	61.5% reported severe peer aggression 46.8% reported experience of peer violence[‡] 70.0% reported violence consequences 34.6% reported any binge drinking 38.1% reported any alcohol misuse (AUDIT-C >= 3) 25.9% reported >= 2 alcohol consequences at 3 months 49.4% reported severe peer aggression 35.1% reported experience of peer violence[‡] 58.7% reported violence consequences 34.1% reported any binge drinking 35.1% reported any alcohol misuse (AUDIT-C >= 3) 21.7% reported >= 2 alcohol consequences at 6 months 52.0% reported severe peer aggression 30.0% reported peer victimization 51.5% reported violence consequences 36.1% reported any binge drinking 34.7% reported any alcohol misuse (AUDIT-C >= 3) 17.3% reported >= 2 alcohol consequences at 12 months

*Article reported to one decimal place; **Explicit values were not given, these rates were read off survival curves provided in Figure 2 of the article; ***There were originally 1,264 individuals, but data on method of self-harm were missing for 51 of these individuals. The authors did not include these 51 individuals when they summarised outcomes of repeat self-harm; † There appears to be an error in reporting the outcome of ‘any experience of peer violence’ at 3 months within Table 2. Have exchanged the n and % values as these mathematically add up. Have contacted the authors to confirm that this is the case.

A.5 Supports for the judgements of levels of risks of bias by domain, for each study included in systematic review

Domain	Prompting iterms for consideration
1. **Study participation**	a. Adequate participation in the study by eligible persons b. Description of the source population or population of interest c. Description of the baseline study sample d. Adequate description of the sampling frame and recruitment e. Adequate description of the period and place of recruitment f. Adequate description of inclusion and exclusion criteria
Study	**Evidence for items for consideration**
Downey 2007 (84)	a. It is not clear how many subjects were approached and how many there were initially for the baseline surveys. Results in tables are given as percentages rather than absolute numbers of participants. b. 'The purpose of this study was to examine whether the SAGE assessment survey could predict, within the Emergency Department setting, those youth at risk for engaging in violent behavior.' c. 'The majority of the subjects in the study were African Americans (60%; n=120), 33% (n= 65) were Hispanic, and 6% (n = 12) Caucasian, with 1% other. They were evenly split with 50% males and 50% females. The subject population was mostly single (92%; n=183), 52% (103) were high school graduates, and 27% (55) had 2 years of high school. However, 20% (n=40) had less than a high school education. The average age was 19 years, with a range of 11–24 years. ' d. 'This study involved young people between the ages of 10 and 24 years who were treated for their injuries in the ED at an urban, level I adult and pediatric trauma center. The data in this study are limited to patients who were admitted to the Emergency Department of the hospital.' 'This was an observation, convenience sample of young male and female patients, half of whom had injuries related to violence and half of whom had injuries unrelated to violence [I only included results for those with injuries related to violence], who presented when a research fellow was available.' e. Period and place of recruitment not reported. f. 'The inclusion criteria were: age 10–24 years, consenting patient or guardian, medically stable, and able to communicate. The exclusion criteria were: those youths who were uncooperative or refused to participate.' 'It excluded patients who received medical care in other areas of the hospital.'

	Comment: There is no information about the research fellow's working times and how they approached participants. Therefore, it is possible that participants were only recruited at convenient times for the research fellow, e.g., weekdays and not evenings or weekends, when adolescents with different related risk factors for harm, e.g., binge drinking, may have presented. It is also not clear how many participants refused to participate, and whether these participants relevantly differed to those who did not refuse. Assessment: Moderate bias
Wiebe 2011 (87)	a. '…131 were eligible, and 95 (72.5%) participated.' b. 'To improve our understanding of risks adolescent patients face and factors that may identify those most needing intervention, we pilot tested an Interactive Voice Response (IVR) survey as a way to accomplish follow-up research with adolescent assault-injured patients.[3]' c. Baseline characteristics described in Table 1. Sixty-three percent of the sample was male, and average of 15 years old, 88% African-American, the majority had A-C grades in school but 80% had ever been suspended. d. 'Clinically-supervised research assistants conducted enrolment.' Sampling frame, e.g., consecutive enrolment, not described. e. 'A prospective cohort study was conducted by interviewing 12-19 year-old patients treated following interpersonal assault (non-partner) in the ED of an urban, university-affiliated, tertiary care pediatric hospital during 2007-2008.' f. '12-19 year olds patients treated following interpersonal assault (non-partner) in the ED… during 2007-2008.' No specific inclusion or exclusion criteria given. Comment: We do not know how the assistants approached participants, or the sampling frame for recruitment. Assessment: Moderate bias.
Cassidy 2009 (75)	a. '112 children presented with Deliberate Self-Harm during the study period. 'Of the 96 families eligible to participate, only 66 families were traceable. 39 parents/guardians (59%) and 10 children agreed to participate in the study.' b. '…aimed to look at rates of repetition in children presenting with Deliberate Self-Harm (DSH) to a paediatric A&E department. c. 'Children presenting with DSH to a paediatric A&E between 2000 and 2005 were invited…' Baseline characteristics of sample described under 'Results' section. 'The mean age at index presentation was 13.28 years (range: 10-18 years). The majority were living at home… …and attending secondary school…2 were in employment and 3 were unemployed. Three females… … reported now having children themselves.' d. No details of sampling frame, who recruited patients, and how. e. 'Children presenting with DSH to a [tertiary] paediatric A&E between 2000 and 2005 were invited to participate in the study.' The exact A&E department not described. f. 'All children who had presented… …with DSH, who were under 18 years old at the time of the follow-up study, were eligible to participate.' 16 children were aged over 18 years at the time of the study and were excluded…'

	Comment: 'As only 10 young people participated, information on repetition rates is mainly based on report from parents who may not be fully aware of all repeat episodes of DSH.' 'It is possible that parents were more likely to participate if their child was doing well and they were happy with their child's mental health. Over one-third of eligible families couldn't be traced. These may have been families with greater problems and therefore where the child lay have had higher risks of repeat self-harm (as may have the families who could be traced but declined to participate). As the authors state above, for those children who did not agree to participate but their parents/guardians did, rates of repeat self-harm may have still been underestimated. Assessment: Moderate bias
Cotgrove 1995 (85)	a. It appears that all adolescents were randomised to receive a token, or not (control group). Therefore, the control group could not refuse to participate. b. 'All adolescents aged 16 years or under, admitted to the study hospitals between January 1987 and January 1990, who made a suicide attempt were included.' 'Seven hospitals and their local child and adolescent departments/clinics in North London were initially included.' c. Description of the baseline study sample at beginning of 'Demographic data' section. 'The female to male sex ratio was approximately 6:1 (n=89:16). The mean age was 14.9 years, with a range of 12.2-16.7 years… …Ninety per cent (n=94) of the suicide attempts… …The commonest "other" factor was sexual abuse which was thought to be significant for four adolescents.' d. See b. 'Patients discharged from hospital following a suicide attempt were randomly allocated…'. No description of the sampling frame or recruitment. It appears that the psychiatrist that would usually assess the child on admission also 'recruited' the patient into the study. However, it also appears that there was no formal recruitment or consent taken. e. See b. 'All adolescents aged 16 years or under, admitted to the study hospitals… …who made a suicide attempt were included. We embraced in our criteria for attempted suicide, all acts of deliberate poisoning and deliberate self-injury.' Comment: There appears to have been no formal recruitment process, and patients may have been recruited by the psychiatrist who was involved in their care and knowledgeable about their history/risk of future harm. Assessment: Moderate bias
Goldston 1999 (73)	a. 'The subjects in this longitudinal study were recruited from a larger sample of 269 adolescents…''To recruit the planned sample of 180 we attempted to locate 225 youths one-half year following their hospitalization. One subject died (of cardiac problems) before he could be asked to participate. We were able to find 96.0% of the remaining pool of eligible subjects; of these 83.7% agreed to participate in the longitudinal study.' b. 'The present study is a prospective, naturalistic, repeated assessment investigation of 180 consecutively referred adolescents after hospitalization.' c. 'The sample for the present study consisted of 91 girls (50.6%) and 89 boys (49.4%)…' 'Youths eligible for the study because they were hospitalized for at least 10 days did not differ from youths with shorter stays in gender and race composition or age at hospitalization.'

	d. 'Sampling was not based on prior history of suicidal behaviour.' 'The subjects in this longitudinal study were recruited from a larger sample of 269 adolescents described at hospitalization in another publication (Goldston *et al*., 1998). To recruit the planned sample of 180 we attempted to locate 225 youths one-half year after their hospitalization.' 'All youths admitted to the inpatient psychiatry unit were assessed during their hospitalization with a standardized battery including semistructured [sic] interview instruments. Thereafter youths were asked to participate in semiannual [sic] follow-up assessments for up to 5 years.' e. 'The 180 adolescents participating in this study were hospitalized between September 4, 1991 and April 10 1995. The youths were recruited from among consecutive discharges from the Adolescent Inpatient Psychiatry Unit of Wake Forest University Baptist Medical Center.' f. 'To be eligible for the study adolescents needed to meet the following inclusionary criteria: (l) ages 12 to 19 years, (2) no evidence of mental retardation, (3) admission to the unit for at least 10 days, (4) no evidence of serious systemic physical disease such as insulin-dependent diabetes mellitus or seizure disorder, (5) still residing in North Carolina or Virginia at the time of the first follow-up assessment (6) not a sibling of a subject already participating in the study and (7) able to cooperate with and complete the inpatient assessment. Comment: High participation rate. The previous study (Goldston *et al*, 1998) states that adolescents were selected from consecutive admissions. In the current study, there is no mention of how the 225 the researchers tried to locate were selected. Assessment: Moderate bias
Granboulan 1995 (77)	a. 'From these various sources, data were collected on a total of 127 subjects, or 48% of the original sample.' b. 'The present retrospective study concerns 265 suicide attempters who had been hospitalised between 1971 and 1980 in the adolescent psychiatric unit of the Salpêtrière Hospital in Paris.' c. 'The initial sample consisted of 64% females and 36% males, mean age 16 years (SD 2.3)…. …psychosis (9%). d. 'All adolescents hospitalized for a suicide attempt between 1971 and 1980, or 265 cases, were included in the study.' 'After a time lapse ranging from 7 to 17 years (mean 11.5; SD 2.7), the subjects were sent a letter explaining the study's aims and asking for an interview, together with a questionnaire inquiring about postdischarge [sic] treatment, any subsequent attempts,… For those subjects who did not return the questionnaire, an attempt was made to obtain the desired information by phone contacts, either with the subjects themselves, their parents or the physician mentioned on their medical record.' e. See b. f. 'All adolescents hospitalized for a suicide attempt… …were included in the study [approached later].' No exclusion criteria given. Comment: Retrospective recruitment. It is likely that those with more chaotic lives (greater psychosocial need) were less likely to be located. The untraced group (over half of the sample) were likely to have had a higher risk of repeat suicide attempt because of a greater likelihood for childhood adversity. Assessment: High bias

Groholt 2006 (78)	a. 'The sample included 87% (N=92) of all adolescents (N=106)…' b. The referenced article (Groholt *et al*, 2000) states that '…in an urban catchment area of approximately 900,000 inhabitants.' c. Table 1 displays baseline characteristics. No clear evidence of unrepresentativeness. d. 'In the present study, a sample of adolescents hospitalized in general hospitals after a suicide attempt was re-examined after approximately 9 years.' 'The adolescents consented to being contacted for a follow-up interview, and they were contacted 8 years later.' No mention of who obtained consent for the later interviews (or how), likely to also have been the first author. e. 'From 1992 to 1994 (T1), 92 adolescents were included in a research project after a suicide attempt.' '…in the Oslo region in Norway during an 18-month period (Groholt, Ekeberg, Wichstrom *et al*, 2000).' The referenced article (Groholt *et al*, 2000) states that 'After a pilot period in 1 hospital, the study included all 6 general hospitals in Oslo and the surrounding counties.' f. '…aged 13 to 19 years who had been admitted to a general hospital for a suicide attempt…' 'This included all nonaccidental, intentional self-harming acts requiring medical care in somatic hospital wards.' No exclusion criteria reported. Comment: High participation rate. Assessment: Low bias
Harrington 1998 (88)	a. 'During the 27-month recruitment phase, a total of 435 young people aged 16 or younger (range 10 to 16 years) who had taken an overdose were referred to the child psychiatry teams.' 'One hundred nine either refused further treatment or refused to enter the trial, or both. Contact was lost with 17 (e.g., absconded from the ward, ran away from home). One hundred sixty-two cases were recruited to the trial and then randomly allocated to either routine care and the home-based family intervention *(n* = 85) or routine care alone *(n* = 77).' b. The 25% (109/435) who refused further treatment or to enter the trial were likely to have had higher risks of harm compared with those that did not. Description of the source population or population of interest c. 'The groups [treatment and control] were well matched on clinical characteristics (Table 1)' but the proportion having used paracetamol to self-poison was slightly higher in the treatment group (62% vs. 51% in the control group) as was the proportion that had a family history of deliberate self-harm (49% vs. 38%). d. 'The study was based on a consecutive series of children and adolescents referred to child mental health teams…' 'All patients referred to the child mental health teams were entered on a register and then assessed by a child psychiatrist and a child psychiatric social worker on the pediatric ward once they had recovered from the physical effects of the overdose. This brief initial assessment was used to determine eligibility for the study and was separate from the first family session.' e. '…referred to child mental health teams working in four hospitals in Manchester, England.'

	f. 'Patients were eligible if they were aged 16 years of younger with a diagnosis of deliberate self-poisoning according to a standard definition (Hawton and Catalan 1982) and if they and their parents or legal guardian gave consent. Referrals with other forms of self-harm such as cutting or attempted hanging were excluded because it was felt they would require other interventions.' '…we wanted to target the group who were most likely to benefit more intervention. Patients were therefore excluded if their social situation precluded a family intervention (e.g. if the child was not living in a family, if the child was in care of social services, or if physical or sexual abuse was being investigated) or if a child psychiatrist decided there was a clinical or psychiatric contra-indication (e.g., if the child had severe mental illness such as psychosis, if the child was currently a psychiatric patient, or if the parent or child had significant learning difficulties or was severely suicidal). Cases in which it was unclear whether the overdose was deliberate or not (e.g., overdose of a drug usually used for kicks, or the adolescent denied that the overdose was deliberate) were also excluded because the intervention program assumes that the overdose is deliberate. Young people with major depression were not excluded because in a previous study in the same hospitals we had shown that major depression after a deliberate overdose resolved rapidly in most cases (Kerfoot *et al*., 1996).' Thirty-eight cases were excluded because they had not taken a deliberate overdose, 48 because they had a psychiatric contraindication, and 61 cases because their social situation precluded a family intervention.' Comment: A lower proportion of family history of self-harm in the control group indicates a potentially lower level of psychological need. That is, there may be some selection bias present in that those with the greatest need were given treatment. This would bias the incidence of outcomes in the control group to be underestimates of outcomes following admission for self-harm in adolescents not participating in any study. Assessment: Moderate bias
Hawton 1999 (89)	a. 'No adolescents refused to be interviewed.' b. 'The aim of this study was to examine the relationship between psychosocial variables and repetition of deliberate self-harm by adolescents (n = 45) aged 13-18 years who had been admitted to a general hospital having taken overdoses.' c. Gender, age and number with previous overdoses described in Table 1. No apparent unrepresentativeness. d. 'The subjects were recruited from consecutive patients…' Consent for interview was obtained from all the adolescents, and from parents for adolescents below the age of 16 years.' '…on the days the research interviewer was available (5-7 days per week)' e. '…admitted to the general hospital in Oxford' f. '…aged 12-18 years residing in Oxford District who were admitted to the general hospital in Oxford because of self-poisoning (not self-injury)…' No exclusion criteria reported. Comment: Highest possible participation rate. Unsure whether patients admitted while research interviewer not present would have different characteristics or outcomes compared to those who admitted while he/she was present. Assessment: Low bias

Hawton 2007 (82)	a. 'All patients who presented to the general hospital in Oxford, United Kingdom, following acts of DSH… …were included in the study.' b. 'Knowledge of risk factors for suicide is a key aspect of prevention of suicide in patients who present with DSH, yet information on such factors in young people is sparse.' 'We have conducted an investigation of the characteristics of a large consecutive series of 15- through 24-year olds who presented to a general hospital during a 20-year period.' c. A total of 5459 individual aged 15 through 24 years, 3432 females (62.9%) and 2027 males (37.1%), presented to the general hospital during the 20-year study period… Just over half were aged 15 to 19 years… with more females… than males… being in this age-group… In all, 4558 (83.5%) received a psychosocial assessment while in the general hospital. More female…patients (N=1602, 79.0%) received and assessment…' Other characteristics described in Tables 1 and 2, but not broken down for 15-19 and 20-24 year olds. I only reported results on 15-19 year olds for the current review. d. See a. e. 'Patients were identified through the Oxford Monitoring System for Attempted Suicide, which collects information on all DSH patients assessed by the general hospital psychiatric service. Nonassessed patients are identified through regular searching of records of presentations to the ED. For these patients, more limited information is collected, including gender, age and methods of DSH.' f. See a. Assesssment: Low bias.
Hawton 2012 (90)	g. 'Data were collected on all patients aged 18 years and under who presented with self-harm to general hospital EDs in Oxford (one), Manchester (three) and Derby (two)…' h. 'Investigate both risk of repetition of self-harm and of suicide following self-harm in children and adolescents, and the factors that are associated with these outcomes. Our overall aims were to provide information relevant to service provision and, especially, for clinical management of young self-harm patients, including assessment of risk.' 'The study was undertaken in three centres currently involved in the Multicentre Study of Self-harm. For further details see (Hawton *et al*., 2007) and (Bergen *et al*., 2010). i. 'Three-quarters (N = 3878, 74.5%) were female. Only four (0.1%) were aged under 10 years (the youngest being 7 years), 929 (17.8%) 10–14 years and 4272 (82.1%) 15–18 years. These individuals were involved in 7150 self-harm episodes which resulted in presentation to the study hospitals during the study period. Of these episodes 5570 (77.9%) involved self-poisoning, 1221 (17.1%) self-injury and 359 (5.0%) both self-poisoning and self-injury (in the same episode).' Descriptive statistics also provided per centre.

	a. See a. ‘Demographic, clinical and hospital management data on each episode were collected by clinicians using standardised forms in Oxford and Manchester. In Derby, data were entered directly into a computerised system by clinicians. Patients not receiving an assessment were identified through scrutiny of ED and medical records (computerised records in Derby), from which more limited data were extracted by research clerks. In all centres, patients not assessed may have taken early discharge, refused the assessment, or not been offered an assessment for clinical reasons or unavailability of staff. Our dual approach to case identification enables us to include all presentations for self-harm to the study hospitals.’ b. ‘Data were collected on all patients aged 18 years and under who presented with self-harm to general hospital EDs in Oxford (one), Manchester (three) and Derby (two) for the 8-year period 1 January to 31 December 2007.’ ‘For examination of repetition we restricted the sample to those individuals who presented between 2000 and 2005 and the follow-up period for repetition to the end of 2007.’ ‘or the mortality follow-up we used the whole 8-year (2000–2007) cohort of patients and followed these up until the end of 2010’ c. See a. ‘At two hospitals in Manchester there was incomplete identification of children under 16 years because they may have attended a separate Children’s ED not included in this study. Children under 16 years who presented to these two hospitals in Manchester may also have been referred elsewhere for psychiatric assessment, thus data was not collected in these cases. This could have affected findings related to repetition of self-harm.’ Assessment: Low bias
Hulten 2001 (76)	a. Not stated. As this is a multi-centre study, have tried to find any related documents for the Oxford dataset in particular. Cannot work out the response rate from these documents. b. ‘The present study sought to identify patterns and risk factors for repetition of attempts in older teenagers.’ ‘Information on attempted suicide in the 15-19 year age group during the period 1989-1995 was analyzed.’ c. Gender, methods used, and previous suicide attempts described. d. ‘…all attempted suicide patients…’ e. ‘All centres registered patients who had attempted suicide and received somatic hospital emergency treatment during the period of study. Other centres were not included in the study because of incomplete data from the follow-up period.’ f. ‘…all attempted suicide patients aged 15 years and over who have received medical health care as a result of their overdose or self-injury.’ No exclusion criteria reported. Comment: Cannot work out who refused to participate. Assessment: Moderate bias

Laurent 1998 (79)	a. Not reported. b. ‘The objective of the present study was to evaluate the long-term outcome of a group of adolescents hospitalized subsequent to attempted suicide, from a catchment area in and around a medium-sized town in the southeast of France.’ c. ‘Of the suicidal subjects for whom information was received, gender was not significantly different, but age was significantly lower than that of suicidal subjects for whom we did not receive information. However, a previous study of characteristics of 122 suicidal adolescents was completed by our research team between 1985 and 1992 (20) [Reference: Foussard *et al*, Synapse 1995]. These subjects were also recruited for the present study, revealing no differences between the 69 respondents and 53 non-respondents in terms of gender, ethnic origin, family situation, size of family, personal and familial psychiatric history (Chi-squared test, *p* . 0.05), and age (Student’s *t*-test, *p* . 0.01). The absence of bias on this subgroup, which represents one third of the suicidal population in the present study (69 of 231), indicates that the nonresponse bias is probably weak.’ No explicit statistics on baseline characteristics. d. No information on who identified these patients and how. e. ‘These were youth admitted into general and emergency pediatric wards, or pedopsychiatry [sic] or clinical toxicology services at the University Hospital of Grenoble, France, between 1982 and 1992.’ f. ‘…children and adolescents,<18 years old and hospitalized following a [sic] attempted suicide.’ No exclusion criteria reported. Comment: It is likely that no significant differences were found in the referenced previous study because the sample sizes were much smaller, rather than there being no real differences in age between responders and non-responders. There is no real *initial* response rate reported because patients were identified by hospital records and only required to respond at follow-up (some responses being retrospective). A lack of reporting on who refused to participate, the sampling frame and recruitment. Assessment: Moderate bias
Rotheram-Borus, 2000 (80)	a. ‘This yielded 167 eligible participants of whom 150 were successfully recruited: Nine were released from the ER before the recruiter could approach them and successfully schedule a follow-up appointment, and eight refused to participate.’ ‘Among the 150 SA [Suicide Attempters] recruited, with informed consent of the SA and their primary caretakers, 10 SA did not complete the baseline assessment, leaving 140 available for the present analysis.’ b. ‘In this report, we examine whether the specialized ER care… … compared with adolescents receiving standard ER care.’ Introduction discusses adolescent suicide attempters, otherwise population of interest not more specifically described. c. Table 1. Slightly lower rates of Latino participants, attempts by poisoning, married mothers, and home-makers in the control group compared to the treatment group. d. ‘When the SA and their parents first entered the ER care (either specialized or standard care), the attending physician rated the lethality of the adolescent's suicide attempt (Pierce Suicide Intent Scale; Pierce, 1977) and level of depressive symptomatology (Hamilton Depression Inventory; Hamilton, 1960), conducted a mental status exam on the adolescent, and gathered socio-demographic information from the adolescent and the parents… Using a quasi-experimental design, this study then assigned SA and their parents to receive either the specialized or standard ER care. Assignment was based on time of presentation to the ER.’

	e. 'The ER at Columbia Presbyterian Medical Center, New York…' '…from March 1991 to February 1994:…' f. 'The eligibility criteria for the SA were: admitted for a suicide attempt to the ER (i.e., had inflicted physical harm to self with a desire to die), aged 12-18 years old, not psychiatrically hospitalized for more than 1 week, female, and not referred to hospitals outside of the New York City area.' '18.6% (n = 87) were male; 26.5% (n = 124) were females identified only as suicidal ideators [sic]; 8.8% (n = 41) were females who were admitted for more than 1 week to a psychiatric ward following the suicide attempt and were unavailable for treatment; 5% (n = 24) were ineligible due to low IQ, wrong age, no parent or family, or having moved immediately out of the area; and 5% (n = 25) were referred to treatment programs closer to their residence.' Comment: High participation rate. However, control group of RCT with an inadequate randomisation method. May have different demographic and medical make up compared with routine identification of all self-harming patients, evidenced by Table 1. Assessment: Moderate bias
Cunningham 2012 (86)	a. 'During the trial, 88.1% (n = 3,784) of the 4296 potentially eligible patients were approached; 3338 completed screening; 829 met study criteria; and 726 completed the baseline survey (see ref 29 for additional details; Fig 1).' b. 'The SafERteens RCT took place at a level I trauma center, Hurley Medical Center; in Flint; Michigan.' 'Adolescent ED patients (14–18 years of age) presenting for medical illness or injury were eligible for screening.' c. Described under 'Sample Description', for the two groups (combined). Appear representative of adolescents presenting to the ED in the US, with violent injury. References Walton *et al* (see Comment below), where comparisons between the three original randomised groups (two were taken forward into this study) showed that those in one of the intervention groups (computer) were statistically significantly more likely to have dropped out of school. The control group were also more likely to have reported past year vilence consequence (98.3% vs. 77.2% and 83.9% in the two intervention groups). d. 'Adolescents were approached from 12 PM to 11 PM, 7 days per week (September 2006 to September 2009), excluding major holidays. Assent/consent by the adolescent, and the parent/guardian if the adolescent was 18 years old, was obtained.' No information on who approached these adolescents and how, however in cited study for further details (55), 'Adolescent patients identified from electronic logs were approached by research assistants in waiting rooms or treatment spaces.' e. See b. and d. f. See b. 'Adolescents seeking care for acute sexual assault or suicidal ideation, altered mental status precluding consent, or who were medically unstable (ie, abnormal vital signs) were excluded.' Comments: Fig 1 in ref 29 (Walton *et al*, JAMA 2010) explains clearly why some eligible participants were not approached, and reasons why 12% did not complete the baseline survey (for the latter, the majority of reasons was discharge/not wanting to stay, no interest in participation, or refusal on the family's part). As major holidays and between 11pm and 12pm (peak times of violent/drinking behaviour) were excluded, a number of adolescents admitted with either aggression and/or alcohol use would have been missed. Cannot be sure whether these adolescents would have been any different to those admitted at other times. Assessment: Moderate bias

Cunningham 2015 (91)	a. Figure 1 is a flowchart describing numbers approached (849 and 846 for AI youth seeking care in the ED and non-AI; 717 and 730 screened; 388 and 278 eligible; 349 and 250 completed baseline), and reasons for not participating at baseline. The majority agreed to return to finish the baseline assessment but did not return. b. 'The purpose of this study was to examine 2-year outcomes of fatal and nonfatal vilent injuries among a sample of assault-injured, srug-using youth (AI group) (14-24 years of age) seeking ED care compared with non-asault-nijured, drug-using youth (non-AI grup) seeking ED care for other reasons.' c. 'Participants were mostly male (58.8%) and African American (58.3%) and received public assistance (73.0%). We found no significant difference between AI and non-AI groups in terms of sex, age, race, and receipt of public assistance.' Also described methods of assault and injury. d. ''Recruitment occurred 7 days per week, 21 h/d (5AMto 2AM) on Tuesday and Wednesday and 24h/d from Thursday through Monday…' 'Assault-injured patients who were medically unstable were recruited on the inpatient unit if they stabilized within 72 hours.' 'Assault-injured youth identified through electronic medical records were approached by trained research assistants (RAs) in waiting rooms or treatment spaces.' 'The non-AI group was enrolled systematically in parallel to the AI group to limit temporal or seasonal variation and was proportionally balanced by age and sex. For example, after identifying a 16-year old female with an acute assault-related injury and drug use in the past 6 months on the screening survey, the RA would recruit sequentially, by triage time, the next female aged 14 to 17 years seeking ED care for a medical complaint or an unintentional injury; those with screen findings that were positive for any drug use in the past 6 months would be recruited for the longitudinal study.' e. '…from December 2, 2009, through September 30, 2011.. f. 'Patients aged 14 to 24 years presenting to the ED for an assault related injury (AI) and a non-AI group proportionally balanced by sex and age (ie, aged 14-17, 18-20, and 21-24 years) who self-reported any drug use in the past 6 months (see the Measures subsection) on a computerized screening survey12 were eligible for inclusion in the longitudinal study. Patients were excluded if they presented for acute sexual assault, child maltreatment (ie, injury caused by an adult caregiver), suicidal ideation/attempt, or conditions precluding ethical consent (eg, altered mental status, psychosis).' Comment: Approximately one-third agreed to participate and returned to fill in a baseline assessment. Those who disagreed or who did not return may have more chaotic lives/adverse outcomes compared to those that did agree/return. Assessment: Moderate bias

Domain	Prompting iterms for consideration
a. Study attrition	a. Adequate response rate for study participants b. Description of attempts to collect information on participants who dropped out. c. Reasons for loss to follow-up are provided. d. Adequate description of participants lost to follow-up. e. There are no important differences between participants who completed the study and those who did not
Study	**Evidence for items for consideration**
Downey 2007 (84)	a. Numbers followed not provided, but from Tables 1 and 2 can work out that there were 84 in the violent injury group at baseline, and 53 were followed up one month (63%) b. Not reported. c. Not reported. d. Not reported. e. Not reported. Assessment: Moderate bias
Wiebe 2011 (87)	a. 'Ninety-five patients were enrolled; 42(44.2%) reported to the IVR survey.' b. From Blackstone *et al* (see Comment): 'Research assistants attempted to contact each subject approximately 4 weeks after his or her enrollment to remind them to utilize the system. RAs used the telephone number(s) provided by subjects at the time of study enrollment. When more than one phone number was provided, all numbers were tried. If the subject could not be reached at these numbers, RAs called the contact number listed in the subjects' medical records. This 4-week call was made irrespective of whether the subject had already accessed the system. RAs were not required to speak to the subject; they were instructed to leave messages on an answering machine or with a family member if necessary. At the conclusion of the study, RAs again attempted to contact each study participant to administer a brief satisfaction questionnaire, to identify barriers to participation and subject retention.' c. Not reported. d. Statistics on sex and age reported.

	e. From Blackstone *et al* (see Comment): 'Contact with the system did not differ by sex (41.7% among males, 48.6% among females, v2 = 0.427, p = 0.513) nor by age group (12–13, 14–15, and 16–18 years; Fisher's exact p = 0.175).' 'Approximately one-quarter (26.3%) of the 19 subjects who were injured in fights involving weapons accessed the system compared to half (50.0%) of the 74 subjects who were not injured in fights involving weapons (Fisher's exact p = 0.075). Approximately one-third (32.3%) of the 31 subjects with initial plans to retaliate accessed the system compared to half (49.2%) of the 63 subjects who did not have initial plans to retaliate (v2 = 2.427, p = 0.119). These differences were not significant.' Comments: 'Details of follow-up have been reported.' Reference Blackstone *et al*, Acad Emerg Med 2009 (different report of the same study). Though differences in proportions of adolescents accessing the system between those fighting with weapons and not, and those that planned to retaliate and those that did not, were not statistically significant, this is probably more due to small sample size. Those involved in weapon fighting and those who planned to retaliate were under-represented in results, and these adolescents are also likely to have the worst outcomes among adolescents with violent injury. Therefore, incidence of violent outcomes was may to be under-estimated. Assessment: Moderate bias.
Cassidy 2009 (75)	a. '39 parents/guardians… …and 10 children agreed to participate in the study.' 'Interviews were conducted with 34 biological parents, 2 adoptive parents and 3 guardians'. In the 'follow-up section: 'Twenty seven participants declined to take part in this study.' If these 27 are children, and 10 agreed to participate, there are two children unaccounted for. b. None reported c. See a. 27 declined to participate but still leaves two unaccounted for. d. 'A comparison was made between responders and non-responders based on clinical information at index presentation. Non responders were less likely to be living at home, more likely to have had a past episode of DSH and more likely to have had a family member with DSH or completed suicide.' No further description, e.g., statistics, on those not followed up. e. See d. Comment: Those who do not live at home, have a past episode of DSH or have a family member with a history of DSH/suicide may have had worse outcomes than other adolescents. Given that non-responders were likely to be adolescents with these characteristics, these characteristics may have been under-represented, and therefore risks of repeat self-harm under-estimated. Assessment: Moderate bias

Cotgrove 1995 (85)	a. 'Twenty-nine cases were excluded from the study [across the treatment and control group (total n = 134), and was not reported separately; maximum possible attrition 29/134 = 22%]' b. Not reported c. '…either because records of the original suicide attempts were missing, or because there were insufficient follow-up data.' d. Not reported e. Not reported Comment: Follow-up was only really possible in the control group if they came back to hospital. Data were collected through hospital notes. Otherwise low proportion of cases excluded. Assessment: Low bias.
Goldston 1999 (73)	a. 'At the cutoff [sic] date for these analyses… …7.2% of the sample (n = 13) had dropped out of the study. b. Not reported. c. See a. d. See e. specific statistics not reported. e. Subjects remaining in our study and subjects who withdrew did not differ in age gender or racial distribution; whether they had attempted suicide within 2 weeks preceding their index hospitalization or had made suicide attempts previously; or in their mean BDI, STAI Trait Anxiety or STAXI Trait Anger scores.' Comment: Low attrition rate. No difference in characteristics between remaining sample and dropouts. Assessment: Low bias.
Granboulan 1995 (77)	a. 'After an average of 11.5 years, 48% of the original sample, or 127 subjects, could be traced.' b. Not reported. c. See a. d. Table of characteristics for those that could be traced and not. e. 'Adolescent variables for the 127 traced [of an initial 265 cases] subjects were then compared to those for the untraced group, using chi-square and Z-tests.' 'This comparison (Table 1) showed three significant differences: 1) fewer divorced parents and 2) more mental disorders in mothers among the traced subjects, and 3) a different diagnostic pattern in the two groups. The traced subjects were more likely to have had a diagnosis of psychosis in adolescence and less likely to have had an adjustment reaction to adolescence than the untraced group.' Comment: Traced subjects were more likely to have mental disorders and a diagnosis of psychosis in adolescence, but less likely to have divorced parents or an adjustment reaction to adolescence, than untraced group. May have biased outcomes, but unclear in which direction. Assessment: Moderate bias.

Groholt 2006 (78)	a. 77% (not including those who died). b. 'We interviewed the parents of four of those who had died, and obtained information about the fifth from medical authorities.' c. 'Of the original 92 adolescents, seven no longer wanted to participate, four were untraceable, three made one or more appointments without turning up, two did not complete the diagnostic interview, five had died, two of them by suicide.' d. 'The 14 adolescents not participating in the follow-up were compared to the 78 participants on all variables in Table 1.' e. 'One difference was found: nonparticipants significantly more often reported a conflict between their parents. Comment: The five who died may not be considered as lost to follow-up, as death may be considered as an outcome. Therefore, 9.8% (9/92) were lost to follow-up without us knowing whether they repeated a (non-fatal) suicide attempt. Though more conflict between parents may suggest a greater likelihood of adverse outcomes in the non-participants, attrition was low, and so any bias in overall results is likely to be negligible. Assessment: Low bias.
Harrington 1998 (88)	a. 'Outcome assessments were conducted with 154 (96%) of 162 cases at 2 months and 149 (92%) of 162 cases at 6 months. b. Not reported. c. Not reported. d. Not reported. e. Not reported. Comment: Many items not reported, but attrition at six months was relatively low (8%). Assessment: Low bias.
Hawton 1999 (89)	a.-f. Not applicable. As outcomes were re-presentations to hospital, we do not know if any participants were lost to follow-up. Comment: It is unlikely that any re-presentations were not captured through the Oxford Monitoring System for suicide, unless any participants represented outside of Oxford. Assessment: Low bias.
Hawton 2007 (82)	a. 'Patients who could not be traced were excluded from the follow-up analyses.' 'Full follow-up until the year 2000 was possible for 4639 patients (85.0% of the original sample). A further 204 (3.7%) were tracked for part of the follow-up period, yielding a total of 4843 individuals (88.7%)… with full or partial follow-up.' Note that these figures are provided for 15-24 year olds, and only results for 15-19 year olds are reported in the current review. b. Not reported. c. 'Patients for whom no information was available (usually because of incorrect identifier information)…'

	d. 'Patients for whom no information was available… …did not differ in gender distribution from those with information. Those with follow-up information, however, were significantly likely to be less than 20 years old (53.1% vs. 46.9%, χ^2=11.8, p<0.001), to have used self-poisoning for DSH (91.0% vs. 86.7%, χ^2=11.8, p<0.001).' e. See d. Comment: Those under 20 years old (the current review's population of interest) were more likely to have information missing and to have self-poisoned. This may indicate greater psychosocial need or a more chaotic life and therefore different risks of outcome. Assessment: Moderate bias.
Hawton 2012 (90)	f. Not applicable. Participants followed using clinical and hospital management data, and the Medical Research Information Services of the NHS. g. 'Patients not receiving an assessment were identified through scrutiny of ED and medical records (computerised records in Derby), from which more limited data were extracted by research clerks. In all centres, patients not assessed may have taken early discharge, refused the assessment, or not been offered an assessment for clinical reasons or unavailability of staff. Our dual approach to case identification enables us to include all presentations for self-harm to the study hospitals.' h. See b. i. Not applicable. See b. j. Not applicable. See a. Assessment: Low bias
Hulten 2001 (76)	a.-f. Not reported. As this is a multi-centre study, have tried to find any related documents for the Oxford dataset in particular. Cannot work out the follow-up rate from these documents. Assessment: Moderate bias.
Laurent 1998 (79)	a. 'Parents could be contacted for 393 suicidal subjects [67% of the 587 who were initially identified] b. 'Responses were obtained from general practitioners for 271 of 378 suicidal subjects (72%)…' 'Information on mortality was obtained for 83% of the suicidal group…' c. '…no address was known for 35 subjects, and 159 others had moved, leaving no forwarding address…' d. Not reported. e. Not reported.

	Comment: A large proportion of families who were identified had moved. Some of these moves may have been related to the suicidal situation of the adolescent and for their family. Two phrases regarding general practitioners state that they completed questionnaires for both 378 and 217 individuals. It may be that this 378/393 is the initial number that could be given a questionnaire, and the 271 is the number that responded. No information on characteristics of group not followed up. Assessment: Moderate bias
Rotheram-Borus, 2000 (80)	a. Follow-up interviews were conducted at 3 (n = 122; 87% follow-up), 6 (n = 118; 84%), 12 (n = 130; 93%), and 18 months (n = 129; 92%) [numbers given here are for treatment and control groups combined] following the date of the initial suicide attempt.' b. Not reported. c. Not reported. d. Not reported. e. Not reported. Comment: The numbers and percentages do not appear consistent. Assessment: Moderate bias.
Cunningham 2012 (86)	a. '…726 completed the baseline survey (see ref 29 for additional details; Fig 1). Of these, the 12-month follow-up rate was 83.6% (n = 607/726) [this is for both treatment and control group].' b. Not reported. c. See Comment. d. Not reported. e. Not reported. Comment: In Figure 1 of this article, the follow-up rate at 12 months for the control group is 86.0% (the 83.6% cited above is for all three groups). Of the 33/235 in the control group who were not followed up at 12 months, 0 had died and 10 had refused. The figure does not explain why the other 23 were not followed up. In the referenced article (Walton *et al*, JAMA 2010), for those lost to follow-up who did not die or refuse to participate, they were labelled as 'incarcerated' or 'lost to follow-up'. Relatively low rates of attrition, and some reasons for loss to follow-up given. Not clear why 23 of the adolescents were lost to follow-up. Assessment: Low bias.

Cunningham 2015 (91)	a. 'The cohort was followed up for 24 months with completion rates of 85.3%, 83.7%, 84.2%, and 85.3% at 6, 12, 18, and 24 months, respectively [this is for both violence and alcohol, and alcohol only group]. b. Not reported. c. Not reported. d. Not reported. e. Not reported. Comment: Relatively low rates of attrition, but no reasons for loss to follow-up given. Assessment: Moderate bias.

Domain	Prompting items for consideration
Prognostic factor measurement	**a. Definition of the PF** **b. Valid and reliable measure of PF** **c. Method and setting of PF measurement**
Study	**Evidence for items for consideration**
Downey 2007 (84)	a. 'The SAGE Baseline Survey measures self-reported use of aggressive and other high-risk behaviours…' 'SAGE was administered to youths presenting due to interpersonal violence (excluding child abuse, sexual assault, and domestic violence)…' Otherwise interpersonal violence not defined. b. 'Prior studies by the authors were referred to in order to differentiate between the two types of injuries [interpersonal violence and non-violent].' Report references Zun *et al*, Pediatric Emergency Care 2005 (268) and Zun *et al*, J Emerg Med 2004 (118). 2004 report states 'presenting to the ED as victims of interpersonal violence with life- or limb-threatening emergencies'. 2005 report states 'a victim of interpersonal violence with life- or limb-threatening emergencies (as determined by the principal investigators LZ).' c. 'However, it has not been tested in a healthcare setting, especially in an Emergency Department. The surveys were conducted by research fellows who were not providing treatment to patients.' It is likely that the identification of adolescents with violent injury was also carried out by these fellows in the ED. Comment: The original purpose of this study was to validate the SAGE questionnaire. The PF in this study (in the context of this review) is the authors' definition of interpersonal violence (see b.), but one is not included either in this report or in the two others referenced. Unclear the level of accuracy of LZ's subjective judgement of violent injury. It is possible that LZ could only identify the most extreme cases of violence, which would result in an over-estimation of the risks of harm in adolescents presenting with violent injury. Assessment: Moderate bias.
Wiebe 2011 (87)	a. '…patients treated after interpersonal assault (non-partner)…' b. Not reported. c. '…in the ED of an urban, university-affiliated, tertiary care pediatric hospital during 2007-2008.' 'Clinically-supervised research assistants conducted enrolment…' Assessment: Low bias.

Cassidy 2009 (75)	a. Not reported b. Not reported c. '…presented to a tertiary paediatric centre between 2000 and 2005 with DSH,' Method for defining DSH not reported. Comment: It is unclear if this includes suspected DSH cases, i.e., including those where there is undetermined intent. Assessment: Low bias.
Cotgrove 1995 (85)	a. '…who had made a suicide attempt were included. We embraced in our criteria, all acts of deliberate self-poisoning and deliberate self-injury.' b. See a. c. 'Every adolescent was assessed by a child psychiatrist on admission.' This was after the adolescent was identified as a suicide attempt, but the report does not say by whom. Comment: Adolescents presenting with self-inflicted injury with undetermined intent do not appear to have been included. Assessment: Low bias.
Goldston 1999 (73)	a. 'Self-destructive behavior was classified as a suicide attempt if it was associated with any desire to die, regardless of multiple motives or ambivalence associated with the act. Self-harm behaviors not associated with intent to kill oneself were not considered to be suicide attempts. Suicidal acts that were stopped before they were executed were considered to be suicidal ideation'rather than suicide attempts. b. 'Suicide attempts were assessed with the Interview Schedule for Children and Adolescents (ISCA) (Kovacs, 1985). Auxiliary information was obtained from interviews with parents, other mental health professionals, behavioral observations, data recorded in medical charts, and prior records.' 'This classification scheme (that described in a.) is similar to that proposed by O'Carroll *et al*. (1996) and has been used previously (Goldston *et al*., 1998, 1999). Results obtained from a previous interrater trial of 46 cases indicated that interrater agreement for the ISCA item regarding suicide attempts (computed as Cohen □) was 1.00 (M. Kovacs, unpublished manuscript, University of Pittsburgh, 1981). A separate interrater trial was conducted as part of the current study. Two raters examined transcribed interviewer notes regarding suicidal behaviors for 40 subjects initially rated as having either suicidal ideation or suicide attempts. The raters (who did not conduct the original interviews and were blind to subjects' identities) independently determined whether subjects had experienced suicidal ideation or attempted suicide. Interrater agreement in classifications of suicidal ideation and attempts was 95% (Cohen □□= 0.90).' c. 'Interviewers using the ISCA were mental health professionals extensively trained in the administration of semistructured interview instruments.' 'All youths were assessed during their hospitalization with a standardized battery including semistructured interview instruments.' Assessment: Low bias

Granboulan 1995 (77)	a. Not reported. b. Not reported. c. Not reported. Comment: From the rest of the report it appears that self-harm with undetermined intent was not included. Assessment: Low bias.
Groholt 2006 (78)	a. See b. b. ‘The participants were asked about suicide attempts since the index suicide attempt. All attempts defined as a suicide attempt by the person in question were included.’ c. Not reported. Comment: It is likely that some adolescents were not entirely honest about their intent when presenting to hospital. It is unclear whether outcomes would have been different for these adolescents, compared to those included in the sample. Assessment: Moderate bias.
Harrington 1998 (88)	a. ‘…a diagnosis of deliberate self-poisoning according to a standard definition (Hawton and Catalan, 1982)…’ ‘Referrals with other forms of self-harm such as cutting or attempted hanging were excluded because it was felt they would require other interventions.’ In Hawton and Catalan (1982)*: “’deliberate self-poisoning’ and ‘overdose’ are used to describe the deliberate ingestion of more than the prescribed amound of medical substances, or ingestion of substance never intended for human consumption, irrespective of whether harm was intended.” b. Neither Harrington (1998) not Hawton and Catalan (1982)* provide a way of measuring deliberate self-poisoning. c. ‘…patients referred to the child mental health teams were entered on a register and then assessed by a child psychiatrist and a child psychiatric social worker on the pediatric ward once they had recovered from the physical effects of the overdose. This brief initial assessment was used to determine eligibility for the study and was separate from the first family session.’ Assessment: Low bias
Hawton 1999 (89)	a. ‘…self-poisoning (not self-injury)…’ b. ‘…Beck Suicidal Intent Scale (Beck *et al*., 1974a): this measure of suicidal intent (wish to die) includes 15 questions on two areas (circumstances and self-report), with each question scored 0±2.’ No measure of (non-suicidal) self-inflicted injury included, report simply says ‘The subjects were recruited from … …because of self-poisoning…’ c. ‘…the research interviewer…’ ‘Each adolescent was interviewed within 24 h of admission.’ Comment: Unclear whether definition included injury with undetermined intent. Assessment: Low bias

Hawton 2007 (82)	a. 'DSH was defined as intentional self-injury or self-poisoning, irrespective of motivation. DSH is a term increasingly used in Europe to describe all acts of self-harm, including both suicide attempts and those with nonsuicidal or mixed intentions. It includes self-mutilation but no stereotypical repetitive acts displayed by individual with developmental disorder or cognitive disabilities.' b. How self-harm was identified is not described. c. The ED. Otherwise identification of self-harm not described. Assessment: Moderate bias
Hawton 2012 (90)	d. 'Self-harm was defined as intentional self-poisoning or self-injury, irrespective of type of motivation including degree of suicidal intent (Hawton, Harriss, *et al*., 2003). This definition, which differs from the binary classification of non-suicidal self-injury and attempted suicide now popular in the USA (Nock, Joiner, Gordon, Lloyd-Richardson, & Prinstein, 2006), is used by most researchers in Europe (Madge *et al*., 2008; Schmidtke *et al*., 1996) and official bodies (National Collaborating Centre for Mental Health, 2004) is based on the fact that motivation for self-harm is often complex (Hawton, Cole, O'Grady, & Osborn, 1982).' e. How self-harm was identified is not described. f. The ED. Otherwise identification of self-harm not described. Assessment: Moderate bias
Hulten 2001 (76)	a. Not reported. b. Not reported. c. 'All centres registered patients who had attempted suicide and received somatic hospital emergency treatment during the period of study…' 'The WHO International Classification of Diseases, tenth revision (ICD-10) (15), was used to classify the methods used in the attempts into 25 different categories. Methods X60-X69 are those that may be designated as "soft", including self-poisoning with medicaments, drugs or other substances. Methods X70-X84 include self-harm of a violent ("hard") nature, i. e. attempted suicide by hanging, jumping or cutting with sharp objects, etc.' These ICD-10 codes only include intentional self-harm. Comment: It appears that final analysis did not include adolescents who presented with injury with undetermined intent. Assessment: Low bias
Laurent 1998 (79)	a. This study defines a suicide attempt as "any act arising from a deliberate wish of self-destruction, no matter whether the intention to die was strong, ambivalent, or very vague" b. References Nielsen *et al*, Acta Psychiatr Scand 1990 and Nordentoft *et al*, Acta Psychiatr Scand 1993, for a. c. Not reported Assessment: Low bias

Rotheram-Borus, 2000 (80)	a. '…admitted for a suicide attempt to the ER (i.e., had inflicted physical harm to self with a desire to die…' b. '…26.5% (*n* = 124) were females identified only as suicidal ideators…[who were ineligible]' '…assessed the SA using the Hamilton Depression Inventory (Hamilton, 1960), the Pierce Suicide Intent Scale (Pierce, 1977), and a mental status exam (Time 0).' These assessments were carried out after suicide attempters were identified. c. See a., judged at ER, probably by physician in department. Comment: It appears that final analysis did not include adolescents who presented with injury with undetermined intent. Assessment: Low bias
Cunningham 2012 (86)	a. 'Adolescent ED patients (14–18 years of age) presenting for medical illness or injury were eligible for screening.' 'Adolescents seeking care for acute sexual assault or suicidal ideation, altered mental status precluding consent, or who were medically unstable (ie, abnormal vital signs) were excluded.' b. 'After completing the 15-minute computerized survey, participants reporting past-year aggressive behaviors (see Measures) and alcohol consumption (ie, consumed alcohol.2 or 3 times in the past year) were eligible for the RCT.' c. 'Past-year alcohol misuse was assessed with the Alcohol Use Disorders Identification Test-Consumption (AUDIT-); with a cutoff of >3 screening positive for alcohol misuse. In addition, the binge-drinking question (5 or more drinks) of the AUDIT-C was examined separately as a binary variable (no/yes).'' Items from the conflict tactic scale assessed past-year severe aggression toward peers (eg, hit or punched, serious physical fighting, used a knife/gun, etc). Severe past-year peer aggression (4 items) was computed as a binary variable (no/yes). Past-year peer victimization (being a victim of moderate or severe peer violence) was assessed by collapsing the moderate and severe conflict tactic scale items into 2 items. A binary variable was then created to indicate if teens reported any peer victimization (no/ yes).' 'Current ED visit reason was abstracted from the medical chart as medical illness (eg, abdominal pain, asthma), or injury International Classification of Diseases–Ninth Revision– intentional [E950–E969] or unintentional [E800–E869, E880–E929]).' Assessment: Low bias.

Cunningham (91)	2015	a. '*Assaults* were defined as any injury intentionally caused by another person…' b. '…self-reported any drug use…' 'Substance use was assessed by using the Alcohol Use Disorders Identification Test and the Alcohol, Smoking, and Substance Use Involvement Screening Tests. Substance misuse was de- fined as meeting criteria for alcohol misuse (Alcohol Use Disorders Identification Test scores of $3 for ages 14–17 years and $4 for ages 18–24 years) or drug misuse (Alcohol, Smoking, and Substance Use Involvement Screening Tests score of $4 for any drug subscales).' c. '…consecutively obtained ED sample of assault-injured youth aged 14-24 years with a history of drug use in the past 6 months (AI group) compared with a group of non–assault-injured, drug-using youth proportionally sampled for age and sex (non-AI group). The study is part of the larger Flint Youth Injury Study.' '…presenting to the ED for an assault related injury and a non-AI group… …who self-reported any drug use in the past 6 months… …on a computerized screening survey were eligible…' From referenced Cunningham *et al*, Pediatrics 2014: Violent injury was 'assessed by RA interview' Comment: Self-reported drug use. It appears that this is through the same computerised survey used to assess all substance use. Both violent injury and drug use may be under-reported/hidden by the adolescent, but no more than would be in our population of interest. Assessment: Low bias.

*The first edition of Hawton and Catalan (1982) was not available through the UCL Library Service. Therefore this quote is taken from the second edition, published in 1987. I have assumed that this definition is remained the same between the two editions.

Domain	Prompting items for consideration
Outcome measurement	a. A clear definition of the outcome is provided b. Method of outcome measurement used is adequately valid and reliable **c.** The method and setting of outcome measurement is the same for all study participants.
Study	**Evidence for items for consideration**
Downey 2007 (84)	a. From Dahlberg *et al*, 2005: SAGE '…measures self-reported recency of aggressive and other high risk behaviors.' b. The purpose of this study is actually to validate the predictive capabilities of the SAGE tool. This study does not confirm how sensitive/specific this tool is. c. 'Follow-up [SAGE] surveys were conducted with each group via telephone after 1 month following their initial visit to the ED.' Comment: References original SAGE survey (Dahlberg *et al*, Division of Violence Prevention, 1998). Could not find this document, but could retrieve the second edition (2005). We do not know how well SAGE surveys pick up aggressive and violent behaviour, e.g., how honest youth are about past behaviours, but these behaviours are likely to be under-reported. Assessment: High bias.
Wiebe 2011 (87)	a. Rather vague: 'Violent experiences'. b. 'Follow-up was accomplished with an Interactive Voice Response survey and randomly assigning patients to report either weekly, bi-weekly, or monthly, over eight weeks following discharge. This involved calling a toll-free number, keying in a self-chosen access password, and keying Yes/No responses to recorded questions about violence-related experiences since discharge or since last reporting.' 'Reported outcomes were assumed to have occurred on the date halfway between the report date and the date the patient was discharged from the ED or last reported.' As there was a toll-free number rather than interviews, participants may have been more likely to answer honestly about aggressive behaviour. However, still may involve some under-reporting. c. See b. Though participants were not assigned to the same time periods for reporting back, this was done at random. Comment: Moderate bias.

Cassidy 2009 (75)	a. Not reported, e.g., whether included all levels of repeat DSH, e.g., cutting or unsuccessful repeat attempts. b. Two methods for picking up outcome: Telephone interviews collected information on demographic details and mental health functioning, including repetition of Deliberate Self Harm.' 'A study specific questionnaire enquired about the child's level of satisfaction… …and any repeat episodes of DSH.' Outcomes may be under-reported. In addition, format of interview and questionnaire not described. c. Not reported. Assessment: Moderate bias.
Cotgrove 1995 (85)	a. 'We embraced in our criteria for attempted suicide, all acts of deliberate poisoning and deliberate self-injury.' b. One year following the suicide attempt information was gathered on use of the green card and on further suicide attempts. Data were collected by reviewing clinic and hospital notes. Other professional were contacted by letter. In all cases this included contacting the general practitioner, and in addition where appropriate; the social worker; educational psychologist or residential unit workers.' c. Information from medical and social contacts may have only been possible for particular adolescents at high risk who come into contact with services. Comment: Some self-harm incidents will not come into contact with medical/social services, so low bias for repeat attempt requiring medical attention, but high bias for all repeat attempts. Assessment: High bias.

Goldston 1999 (73)	a. 'Self-destructive behavior was classified as a suicide attempt if it was associated with any desire to die, regardless of multiple motives or ambivalence associated with the act. Self-harm behaviors not associated with intent to kill oneself were not considered to be suicide attempts. Suicidal acts that were stopped before they were executed were considered to be suicidal ideation rather than suicide attempts.' b. 'Thereafter youths were asked to participate in semiannual [sic] follow-up assessments for up to 5 years.' 'For the follow-up assessments the full ISCA [Interview Schedule for Children and Adolescents] was administered to both the adolescents and adult informants (until subjects were age 18 or living independently). Auxiliary information was obtained from school treatment, and legal records. Psychiatric diagnoses were made on the basis of all available information discussed in conference, and determined by consensus.' 'Suicide attempts were assessed with standardized ISCA questions (e.g., "Have you ever thought about killing yourself?") and corresponding predefined rating scales. Results obtained from an interrater trial of 46 cases indicated that interrater agreement for the ISCA item regarding suicide attempts (computed as Cohen K) was 1.00 (M. Kovacs, unpublished manuscript, University of Pittsburgh, 1981).' 'To determine whether subjects with whom we had lost contact had died we searched the publicly available National Death Index.' c. Approximately half of these interviews took place in the medical center; the remainder were scheduled off-site in subjects' homes residential treatment facilities hospitals, group homes, prisons, and training schools.' Comment: Suicide attempts likely to be under-reported, but all suicides to completion will have been captured. Assessment: Moderate bias for suicide attempts, low bias for death.
Granboulan 1995 (77)	a. Not reported. b. The subjects were sent a letter… …asking for an interview, together with a questionnaire inquiring about postdischarge treatment, any subsequent attempts… …For those subjects who did not return the questionnaire, an attempt was made to obtain the desired information by phone contacts, either with the subjects themselves, their parents or the physician mentioned on their medical record.' 'No death certificate search could be performed for the untraced subjects.' c. Heterogeneous methods between subjects: 'From these various sources, data were collected on a total of 127 subjects, or 48% of the original sample. Twenty-four subjects completed the questionnaire, and 12 of them accepted a personal interview. Twenty-two more accepted a phone interview. For 54 subjects, information was provided by parents, and for 27 by their physicians.' Comment: Not clear whether suicide attempts included acts that were stopped before execution were included or not. Assessment: High bias for suicide attempts, low bias for death.

Groholt 2006 (78)	a. No: ‘All attempts defined as a suicide attempt by the person in question were included…’ b. ‘The participants were asked about suicide attempts since the index suicide attempt. All attempts defined as a suicide attempt by the person in question were included, and the approximate date was noted. Follow-up with regard to death or emigration was performed by linkage to the Population Registry of Norway. Cause of death was given by parents or by medical records.’ c. Not mentioned who contacted the adolescents and how (e.g., letter, telephone), so also unclear if methods homogenous between patients. Also unclear which outcomes were retrieved from the therapist. Comment: Suicide attempts likely to be under-reported, and potentially completed suicides, as cause of death provided by parents. Assessment: Moderate bias for repeat suicide attempts, low bias for death.
Harrington 1998 (88)	a. There were primary outcomes of suicidal ideation and hopelessness and several secondary outcomes. We were interested in repeat self-harm during follow-up (one of the secondary outcomes). b. ‘Both groups were assessed at the time of recruitment and 2 and 6 months later.’ ‘The primary outcome measures were validated in a pilot study conducted by the two outcomes assessors (Kerfoot *et al*., 1996) and comprised the Suicidal Ideation Questionnaire (Reynolds, 1988) and the Hopelessness Questionnaire (Kazdin *et al*., 1986) completed *by* the patients, and a questionnaire measure of family functioning completed independently *by* both the patient and the parents) (Miller *et al*., 1985). Secondary outcome measures were the Generation of Alternative Solutions subscale of the Social Problem Solving Inventory (Sadowski and Kelley, 1991), which was completed by the child; the 28-item version of the General Health Questionnaire (Goldberg. 1978), a measure of stress completed by the parenrts): and 8-point Likert scales of satisfaction with treatment completed by the child and parentis) (Wood *et al*., 1996). The children's and parents' expectancies of treatment were also assessed on a 0 to 8 Likert scale.’ Not clear how repeat self-harm picked up. c. No mention of where these assessments took place. Appears that the assessments were the same for all parents and children. Comment: Repeat self-harm may have been under-estimated (which was more likely if only the children were questioned about self-harm rather than both children and parents). It also depends whether repeat self-harm was part of the questionnaires, or picked up as repeat self-harm leading to hospital visits. Likely to be the former. Assessment: Moderate bias.

Hawton 1999 (89)	a. Repetition of deliberate self-harm (self-poisoning or self-injury) b. ‘Repetition of deliberate self-harm (self-poisoning or self-injury) during the year following entry to the study was identified by the Oxford Monitoring System for Attempted Suicide (Hawton *et al*., 1997). It included general hospital referral because of deliberate self-poisoning or self-injury, irrespective of whether this resulted in admission. Episodes not resulting in hospital referral and those occurring away from the catchment area would not have been identified.’ c. The method and setting of outcome measurement is the same for all study participants, except those who are likely to be referred outside of Oxford, which is likely to be a negligible proportion. Comment: Would not capture any repeat self-harm that did not result in a re-presentation to hospital. Quote: High bias
Hawton 2007 (82)	a. ‘We have also followed up these individuals to examine deaths from all causes, including suicide and risk factors associated with this outcome.’ All deaths that received a coroner’s verdict of “suicide” (ICD-9 codes E950-E959), “undetermined cause” (E980-E989, excluding E988.8), or “accidental poisoning” (E850-E869) were combined to form a “probable suicide” category, as it has been shown that overall mortality form suicide will be underestimated if the verdict of suicide alone is used.” b. See a. ‘Demographic information… for all patients… was submitted to the Office of National Statistics for England and Wales, the Central Services Agency in Northern Ireland, and the General Register Office for Scotland. Tracing revealed whether a patient was alive or decreased as of December 31, 2000.’ c. See b. Assessment: Low bias.

Hawton 2012 (90)	d. '…to investigate both risk of repetition of self-harm and of suicide following self-harm…' 'Data on repetition of self-harm were based on re-presentations for further self-harm to the hospital where the initial episode by each individual during the study period was identified.' 'Mortality information was supplied by the Medical Research Information Services of the NHS (MRIS), which traced and flagged individuals using the Central Health Register Inquiry System for patients in the UK, and equivalent sources in Scotland.' 'ICD-10 codes for the underlying cause of death were grouped as follows: intentional self-harm, X60-X85…' e. Justification for choice of ICD codes to identify self-harm (and repeat self-harm) not discussed. '…suicide was defined as death where the underlying cause of death was intentional self-harm or undetermined intent. This is in keeping with UK national policy on suicide statistics (Department of Health, 2002).' f. 'Demographic, clinical and hospital management data on each episode were collected by clinicians using standardised forms in Oxford and Manchester. In Derby, data were entered directly into a computerised system by clinicians. Patients not receiving an assessment were identified through scrutiny of ED and medical records (computerised records in Derby), from which more limited data were extracted by research clerks.' The method and setting of outcome measurement was the same for all study participants for mortality outcomes. Assessment: Low bias
Hulten 2001 (76)	a. Not reported but does state: 'The WHO International Classification of Diseases, tenth revision (ICD-10) (15), was used to classify the methods used in the attempts into 25 different categories. Methods X60-X69 are those that may be designated as "soft", including self-poisoning with medicaments, drugs or other substances. Methods X70-X84 include self-harm of a violent ("hard") nature, i. e. attempted suicide by hanging, jumping or cutting with sharp objects, etc.' b. Not stated. As this is a multi-centre study, have tried to find any related documents for the Oxford dataset in particular. Cannot work out the method for capturing outcome, from these documents. However, suspect this study uses the Oxford Monitoring System for Attempted Suicide. c. Not reported. Assessment: Moderate bias

Laurent 1998 (79)	a. Mortality and repeat attempted suicide: This study defines a suicide attempt as "any act arising from a deliberate wish of self-destruction, no matter whether the intention to die was strong, ambivalent, or very vague" b. 'Evaluation took place by means of mailed questionnaires completed by the adolescents, their parents, and the general practitioner.' 'Parents and subjects were sent two separate but similar questionnaires delivered in the same envelope addressed to the parents.' 'When both parents and child had answered their questionnaire, only the child's questionnaire was taken into account. In all but five cases, responses from the parents and their child were similar.' 'Psychiatric hospitalizations since the indexed attempted suicide, psychiatric consultations, and psychotropic medications were measured with simple "yes" or "no" responses.' 'Mortality rates were ascertained either from departmental registers (for 436 suicidal subjects [of the initial 587 identified] or from the parents and/or adolescents and/or general practitioners (for 49 suicidal subjects [of the 393 that could be contacted]…' c. For each subject, some had parents who responded, and some did not. Comment: Departmental registers picked up mortality rates in a substantial proportion of subjects, but not all (83%). For non-mortality outcomes, child questionnaire responses were prioritised and will have likely been more sensitive for picking up all incidences of a repeat suicide attempt than use of hospital data for related re-presentations alone. Incidence of repeat suicide attempts may have been under-estimated, but not mortality (including completed suicide). Assessment: Moderate bias for suicide attempts and death
Rotheram-Borus, 2000 (80)	a. Suicide attempt: '…i.e., had inflicted physical harm to self with a desire to die…' a. 'At each SNAP therapeutic session, as well as at each follow-up assessment, self-reports were gathered from the SA and their mothers reporting any new suicide attempts (self-injury with an intent to die that required medical attention) or reideation by the SA. Suicidal reideation was asked as a yes or no event of thinking seriously about killing oneself for a period of 2 weeks.' 'The records in the ER at Columbia Presbyterian Medical Center were monitored to identify all admissions for suicide attempts among the sample…' 'The Columbia Presbyterian Medical Center was the predominant provider in the area; it is unlikely that SA received care at any other facility during the follow-up period.' b. No information about whether all mothers were picked up. Comments: Suicide attempts may have been under-estimated because respondents did not answer truthfully and are likely to be under-estimated because not all will have resulted in admission. Assessment: High bias

Cunningham (86)	2012	a. '…violence (peer aggression, peer victimization, violence-related consequences) and alcohol (alcohol misuse, binge drinking, alcohol related consequences).' b. 'The 12-month follow-up data were obtained via self-administered computer survey.31–33 [sic] Twelve-month surveys were completed in the same manner as the 3- and 6- month follow-ups, at the ED or at a convenient location (eg, home, library, or restaurant);' From referenced study (Walton *et al*, JAMA 2010): 'Follow-up staff were blinded to baseline condition assignment.' c. The method and setting of outcome measurement was unlikely to have been the same for all study participants given the different locations, but method may have been similar given that staff were blinded. Comment: Outcomes likely to have been under-estimated by self-report. Assessment: High bias
Cunningham (91)	2015	a. '*Assaults* were defined as any injury intentionally caused by another person' (definition of PF but also one of the outcomes). b. 'Assault-related reinjury for which the participant sought ED care was examined as a composite measure that captured medical record data on ED visits at the study health system during the 24- month follow-up and self-report data from each of the 6, 12, 18, and 24-month follow-up surveys (to capture visits that may occur out of the study ED).' 'Out-of-hospital mortality was assessed through family members during attempted follow-up contact, local media, and regular review of national and local public health mortality records.' 'Medical records were audited with an error rate of less than 5%.' 'A prior study found that 90% of this sample uses the study site hospital system exclusively for routine medical care.' c. The method and setting of outcome measurement was the same for all study participants. Comment: Violent injury may have been under-estimated through survey and will have been under-estimated by repeat ER visits (a way of picking up false responses in surveys). Mortality is unlikely to have been under-estimated. Assessment: Moderate bias for violent injury, low bias for death

Domain	Prompting items for consideration
Statistical analysis and reporting	g. There is no selective reporting of results. h. Analyses take different lengths of follow-up into account. i. Results are reported with confidence intervals, or at least numbers and proportions can be used to estimated confidence intervals post-report.
Study	**Evidence for items for consideration**
Downey 2007 (84)	a. All items reported (survey is of 12 items). b. All participants followed up at exactly 1 month. c. Numbers and proportions reported. Assessment: Low bias
Wiebe 2011 (87)	a. Does not appear so: 11 outcomes in survey and 11 reported at the end. b. '42 (44.2%) patients completed at least one IVR report during follow-up and 13.7% made all requested reports.' 'IVR data were analyzed using the product limit method and 95% confidence intervals (CI) to estimate the cumulative risk (ie, 1-survival) of each outcome within four and eight weeks of ED discharge.[6]' c. See b. Assessment: Low bias
Cassidy 2009 (75)	a. Does not appear so. The primary outcome was stated as repetition of deliberate self-harm. b. 'Duration of follow-up ranged from 1-6 years'. c. Numbers and proportions reported, but at times was not clear how many were in the denominator: 96 families were recruited, 66 were traceable and 27 declined to take part at follow-up. Assessment: High bias.

Cotgrove 1995 (85)	a. Does not appear so. The primary outcome was stated as repetition of suicide attempt. b. The outcome for all participants were reported for one year after the index presentation. No deaths were reported, so assumed that number at beginning were followed up. c. Numbers and proportions reported. Assessment: Low bias
Goldston 1999 (73)	a. Does not appear so. The primary outcome was stated as repetition of suicide attempt. b. 'Graph of survival curves presented. c. Survival curves presented with confidence intervals. Assessment: Low bias
Granboulan 1995 (77)	a. Does not appear so. The primary outcome was stated as repetition of suicide attempt. b. Data were collected on 48% of subjects. Different lengths of follow-up (an average of 11.5 years), but only numbers and proportions reported. c. See b. Assessment: High bias
Groholt 2006 (78)	a. Does not appear so. The primary outcome was stated as repetition of suicide attempt. b. Different lengths of follow-up (average: 109, range: 90-126 months). Methods from survival analysis were used, Kaplan-Meier for plotting and Cox regression to analyse the risk of later suicidal acts, including attempts and completed suicide…' c. No confidence intervals presented with Kaplan Meier curves, but numbers and proportions of suicide attempts (by the end of follow-up) are reported (so could calculate confidence intervals whilst not taking into account different lengths of follow-up). Assessment: Low bias (when using survival curves and not including confidence intervals)
Harrington 1998 (88)	a. Does not appear so. The primary outcome was stated as repetition of suicide attempt. b. 'Outcome assessments were conducted with 154 (96%) of 162 cases at 2 months and 149 (92%) of 162 cases at 6 months.' High follow-up to 6 months, but some will not have contributed to the numbers and proportions in c. c. Numbers and proportions reported. Assessment: Moderate bias

Hawton 1999 (89)	a. Reported one-year repeat rates for those in 2000-2006, but not clear if this period of one year decided pre- or post-hoc. b. Patients had different lengths of follow-up. 'Of children and adolescents who presented to the hospitals in the three centres with self-harm each year between 2000 and 2006 (N = 5,096), an average of 17.7 % represented to hospital following a further self-harm episode within 12 months.' c. Rates were calculated (with 95 % confidence intervals) for each centre. Assessment: High bias
Hawton 2007 (82)	a. Does not appear so. Outcomes of death, all and by cause, are reported in great detail. b. Time-to-event methods were employed for 15-24 year olds, but not the sub-group of 15-19 year olds. Only the latter results were extracted for the current review. c. Confidence intervals were provided, but as for b. Assessment: High bias
Hawton 2012 (90)	d. 'Univariate models (entry of one predictor variable only) were determined initially. Independent predictors were estimated from multivariate models using entry of all variables significant in univariate models at $p < 0.2$.' Perhaps selective. Choice of 0.2 appears quite arbitrary. e. 'Hazard ratios were estimated from Cox proportional hazard models' f. No confidence intervals presented with Kaplan Meier curves, but numbers and proportions of repeat self-harm and suicide attempts (by the end of follow-up) are reported (so could calculate confidence intervals whilst not taking into account different lengths of follow-up). Assessment: Moderate bias
Hulten 2001 (76)	a. Does not appear so. The primary outcome was stated as repetition of suicide attempt. b. 'The mean follow-up period was 204 weeks (SD 108.9) (approximately 3.9 years), 208 weeks (SD 107.7) for males and 203 weeks (SD 109.4) for females. The longest follow-up period was seven years. Of 1,264 individuals, 217 (66 males and 151 females), or 17.2% of the whole group made repeat attempts during the follow-up period.' Survival curves presented across the whole group. c. No confidence intervals presented with Kaplan Meier curves, but numbers and proportions of suicide attempts (by the end of follow-up) are reported (so could calculate confidence intervals whilst not taking into account different lengths of follow-up). Assessment: Low bias (when using survival curves and not including confidence intervals)

Laurent 1998 (79)	a. Does not appear so. The primary outcome was stated as repetition of suicide attempt. b. ‘The time delay from the first indexed attempted suicide was 6 months in 34% of cases, ,1 year in 51% of cases, and ,2 years in 77% of cases.’ c. Numbers and proportions are reported, but only 282/587 of suicidal subjects were traced, so confidence intervals could be estimated for proportions but only whilst not taking into account different lengths of follow-up. Assessment: High bias
Rotheram-Borus, 2000 (80)	a. Unsure. Repeat suicide rates were reported as an aside. b. Different lengths of follow-up. ‘The cumulative rate of first re-emergence of suicidal ideation rate was: 3 months—14.5%; 6 months—23.1%; 12 months—27.9%; 18 months—29.8%.’ These rates appear to have not been calculated using survival analysis methods as none of this is mentioned in the statistical analysis section. The main purpose of the study was to compare differences between suicide attempters and controls, and to estimate associations of other factors, so the analysis section does not discuss how repeat rates were calculated. c. No confidence intervals reported. Proportions reported but denominator not clear. Assessment: High bias
Cunningham 2012 (86)	a. Does not appear so. Outcomes reported match those in the Methods section. b. Outcomes reported for all adolescents at one year. ‘An intent-to-treat approach was used. All randomly assigned participants were included whether the intervention was received or not (>95% received their assigned intervention during the ED visit).’ c. Numbers and proportions reported. Assessment: Low bias
Cunningham 2015 (91)	a. Unsure. The authors report slightly different range of outcomes to that in 2012. b. Different lengths of follow-up. Kaplan-Meier (nonparametric) estimators of the survival function for the AI and non-AI groups were plotted with confidence bands c. See b. Assessment: Moderate bias

B. Overview of systematic review of interventions to reduce harm in adolescents with adversity

B.1 Search terms

For systematic reviews of RCTs in individuals exposed to violence, self-harm or drug/alcohol misuse:

(“adolescen”* OR “child*” OR “young” OR “youth” OR “juvenile” OR “teen*”)[Title] AND (“victim*” OR “assault” or “maltreat”* OR “violence” OR “self-harm” OR “suicid*” OR “self-injury” OR “substance” OR “drug*” OR “alcohol” OR “drink”)[Title] AND (“review” OR “meta-analysis”)[Title] AND ("1995/01/01"[Date - Publication] : "2015/01/31"[Date - Publication])

For reports of individual RCTs in adolescents exposed to violence:

(“adolescen”* OR “child*” OR “young” OR “youth” OR “juvenile” OR “teen”*)[Title] AND (“victim”* OR “assault” or “maltreat*” OR “violence” OR “abuse”*)[Title] AND (“intervention” OR “prevention” OR “program”* OR “evaluat”* OR “trial” OR treat”*)[Title] AND ("2006/06/01"[Date - Publication] : "2015/01/31"[Date - Publication])

For reports of individual RCTs in adolescents exposed to self-harm:

(“adolescen”* OR “child”* OR “young” OR “youth” OR “juvenile” OR “teen”*)[Title] AND (“self-harm” OR “suicid”* OR “self-inj”*)[Title] AND (“intervention” OR “program”* OR “prevention”)[Title] AND (“evaluat”*” OR “trial” OR treat*”)[Title] AND ("2009/01/01"[Date - Publication] : "2015/01/31"[Date - Publication])

For reports of individual RCTs in adolescents exposed to drug/alcohol misuse:

(“adolescen”* OR “child”* OR “young” OR “youth” OR “juvenile” OR “teen”*)[Title] AND (“substance”* OR “drug*” OR “cannabis” OR “marijuana” OR “opiate”* OR “opioid”* OR “ecstasy” OR “solvent”* OR “cocaine” OR “addict”* OR “alcohol” OR “drink” OR “drunk” OR “intoxicat”* OR “narcotic”* OR “amphetamine”*)[Title] AND (“intervention” OR “prevention” OR “program”* OR “evaluat”* OR “trial” OR treat”*)[Title] AND ("2013/09/25"[Date - Publication] : "2015/01/01"[Date - Publication])

For reports of individual RCTs in adolescents exposed to violence, self-harm, or drug/alcohol misuse (within ISRCTN.com):

("adolescen*" OR "young" OR "youth" OR "juvenile" OR "teen") within Date applied: from: 31/01/2013 Date applied: to: 31/01/2015 Condition Category: Mental and Behavioural Disorders OR Not Applicable OR Injury, Occupational Diseases, and Poisoning OR Not Specified

For reports of individual RCTs in adolescents exposed to violence, self-harm, or drug/alcohol misuse (within ClinicalTrials.gov)

("adolescen*" OR "young" OR "youth" OR "juvenile" OR "teen") | Interventional Studies | (“Aggression” OR “Self-injurious Behaviour” OR “Suicide” OR “Suicide Attempt” OR “Alcohol Drinking” OR “Alcohol-related Disorders” OR Alcohol Dependence” OR "Drug Overdose" OR “Substance-related Disorders” OR “Wounds and Injuries”) | Child, Adult | received from 01/31/2013 to 01/31/2015

B.2 RCTs of interventions* that were registered with ISRCTN.com or ClincalTrials.gov**, and met inclusion criteria of overview

Title	Author, Location	Intervention	Recruitment	Outcomes measured	Status	Project ID
A Brief Intervention to Prevent Adolescent Dating Aggression Perpetration (PLR)	Boston University	Brief intervention	16-18 year olds presenting to paediatric emergency department with aggressive behaviours	Dating aggression perpetration at 3 and 6 months	Not yet open	NCT02080 923
Building Resilience and Attachment in Vulnerable Adolescents (BRAVA)	Allison Kennedy, Children's Hospital of Eastern Ontario	Behavioural Group Intervention (6 psycho-educational group sessions for carers and 6 separate sessions for adolescents)	13-17 year old presenting to emergency department in response to psycho-social crisis	Suicidal ideation, familial support, coping strategies, depression and anxiety at 6 weeks	Recruiting	NCT01925 807
Brief Intervention for Suicide Risk Reduction in High Risk Adolescents (ASAP)	David Brent, University of Pittsburgh	Motivational interviewing, development of a safety plan and treatment modules to target specific individual needs	12-17 year olds admitted to an inpatient unit for a recent suicide attempt or significant suicidal ideation with a plan or intent.	Suicidal ideation and behaviour, treatments, client satisfaction/thoughts on intervention through qualitative interviews, at 4, 12 and 24 weeks	Recruiting	NCT02272 179
Developing and evaluating interventions for adolescents with alcohol use disorders who present through emergency departments: randomised feasibility study and exploratory randomised controlled trial	Dr Paolo Deluca, Kings College London	Screening + either 1) smartphone-delivered brief intervention, or 2) face-to-face brief advice from a trained research assistant	14-18 years olds who own a smartphone and present to emergency department with alcohol misuse.	Drinking behaviours measured by the Timeline Follow Back 28 days interview, at 12 months	Completed, results not yet available	ISRCTN45 300218

Skills to Enhance Positive Affect in Suicidal Adolescents (STEP)	Shirley Yen, Brown University	Positive Affect Skills training (4 sessions)	12-18 year olds admitted to hospital due to concern of suicide risk, who live at home	Task scores relating to affect suicidal ideation, depression and hopelessness, at 1 and 4 months.	Recruiting	NCT02130583
Wrap Around Care for Youth Injured by Violence	Dr. Carolyn Snider, University of Manitoba	On call support worker with lived experience with violence, supported by a social worker, an addictions and mental health counsellor, a family counsellor and links to multiple community partners.	Presentation with an injury caused by violence (defined as an injury inflicted by someone else and one of a gunshot wound, stab wound, injury due to blunt object, or injury due to bodily force). Age 14-24	Pilot study: recruitment feasibility, fidelity to treatment, adherence, repeat injuries/hospital visits, serious adverse events, cost-effectiveness, over the following 2 years	Completed, results not yet available	NCT01895738

*to reduce harm in adolescents after a presentation to the emergency department with adversity
**date registered 31/01/13 to 31/01/15

B.3 A measurement tool to assess the methodological quality of systematic reviews (the AMSTAR tool)

Question	Notes*
Was an 'a priori' design provided?	The research question and inclusion criteria should be established before the conduct of the review. Note: Need to refer to a protocol, ethics approval, or pre-determined/a priori published research objectives to score a "yes."
Was there duplicate study selection and data extraction?	There should be at least two independent data extractors and a consensus procedure for disagreements should be in place. Note: 2 people do study selection, 2 people do data extraction, consensus process or one person checks the other's work.
Was a comprehensive literature search performed?	At least two electronic sources should be searched. The report must include years and databases used (e.g., Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found. If at least 2 sources + one supplementary strategy used, select "yes" (Cochrane register/Central counts as 2 sources; a grey literature search counts as supplementary).
Was the status of publication (i.e. grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.	If review indicates that there was a search for "grey literature" or "unpublished literature," indicate "yes." SIGLE database, dissertations, conference proceedings, and trial registries are all considered grey for this purpose. If searching a source that contains both grey and non-grey, must specify that they were searching for grey/unpublished lit.
Was a list of studies (included and excluded) provided?	Acceptable if the excluded studies are referenced. If there is an electronic link to the list but the link is dead, select "no."
Were the characteristics of the included studies provided?	In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioe-conomic data, disease status, duration, severity, or other diseases should be reported. Acceptable if not in table format as long as they are described as above.

Was the scientific quality of the included studies assessed and documented?	'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant. Can include use of a quality scoring tool or checklist, e.g., Jadad scale, risk of bias, sensitivity analysis, etc., or a description of quality items, with some kind of result for EACH study ("low" or "high" is fine, as long as it is clear which studies scored "low" and which scored "high"; a summary score/range for all studies is not acceptable).
Was the scientific quality of the included studies used appropriately in formulating conclusions?	The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations. Might say something such as "the results should be interpreted with caution due to poor quality of included studies." Cannot score "yes" for this question if scored "no" for question 7.
Were the methods used to combine the findings of studies appropriate?	For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e., Chi-squared test for homogeneity, I^2). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?). Indicate "yes" if they mention or describe heterogeneity, i.e., if they explain that they cannot pool because of heterogeneity/variability between interventions.
Was the likelihood of publication bias assessed?	An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test, Hedges-Olken). If no test values or funnel plot included, score "no". Score "yes" if mentions that publication bias could not be assessed because there were fewer than 10 included studies.
Was the conflict of interest included?	Potential sources of support should be clearly acknowledged in both the systematic review and the included studies. To get a "yes," must indicate source of funding or support for the systematic review AND for each of the included studies.

*Notes from Shea *et al*. BMC Medical Research Methodology 2007 (94), and Michelle Weir, Julia Worswick, and Carolyn Wayne, 'based on conversations with Bev Shea and/or Jeremy Grimshaw in June and October 2008 and July and September 2010' (http://amstar.ca/docs/AMSTARguideline.pdf).

B.4 Characteristics of systematic reviews of RCTs of interventions to reduce harm after adversity not included in overview*

Lead author, year	Scope of review	Time period for search	Databases searched	Number of studies retrieved	Number of RCTs meeting inclusion and exclusion criteria for current review
Population of interest: Individuals exposed to violence					
Limbos 2007 (97)	Primary, secondary and tertiary interventions for preventing youth violent behaviour.	1990 to May 2006	'The National Library of Medicine performed all searches'. No other details given in report.	41	None
Population of interest: Individuals exposed to self-harm					
Crawford 2007 (269)	Psychosocial interventions following self-harm, to reduce risk of subsequent suicide.	1966 to Feb 2005	Keyword search (based on Hawton 1998) in EMBASE, Medline and PsycINFO	18	2: Harrington 1998, Wood 2001
Daniel 2009 (270)	Psychosocial interventions for reducing or preventing the recurrence of adolescent suicidal behaviour.	Until Jul 2008	Medline and PsycINFO	12	5: Cotgrove 1995, Donaldson 1995, Harrington 1998, King 2006, Wood 2001
De Silva 2013 (271)	Intervention to prevent and treat suicide and self-harm in young people	1980 to Jan 2011	CENTRAL, EMBASE, MEDLINE, PsycINFO	38, and 6 reviews	None
Gould 2003 (272)	Research on youth suicide	Not reported. Reviewed 'past 10 years' and article accepted in 2002.	Education Full Text, ERIC, Medline, PsychINFO	Not reported (search was for all research on youth suicide)	2: Cotgrove 1995, Harrington 1998

Hawton 1998 (273)	Interventions for patients who have deliberately harmed themselves.	Until May 1996	Cochrane Controlled Trials Register, EMBASE, Medline, PsycLit, "10 journals in the specialty of psychiatry and psychology that had not been searched within the Cochrane Collaboration, including all the English language journals concerned with suicide".	20	1: Cotgrove 1995
MacGowan 2004 (274)	Interventions for suicidal adolescents	Until December 2002	Campbell Collaboration's Social, Psychological, Educational and Criminological Trials Register, the abstracts of Cochrane Reviews, Psychinfo, PubMed, and Social Work Abstracts.	10	3: Cotgrove 1995, Harrington 1998, Wood 2001
Milner 2015 (275)	Brief contact interventions (letters, green cards, postcards) for reducing the incidence of repeat self-harm and suicide	Not reported. Article first received 13th Feb 2014.	CENTRAL, EMBASE, Medline	20 articles for 14 distinct studies	1: Cotgrove 1995
Steele 2007 (276)	Literature on suicide in children and adolescents	1966-2007	EMBASE, MEDLINE, and personal databases and colleagues (SUICDATA, YouthSuicRandom2004, Youth2)	Not reported (search was for all research on youth suicide)	5: Donaldson 1995, Harrington 1998, King 2006, Spirito 2002, Wood 2001
Population of interest: Individuals exposed to drug/alcohol misuse					
Calabria 2013 (277)	Interventions outside educational settings, for young people with existing alcohol use problems or who are at high risk.	2005-2009	ACP Journal Club, CDSR, CCTR, DARE, EMBASE, ERIC, Medline, Project Cork, PSYCInfo, Web of Science	9	None
Clark 2010 (278)	Screening and BIs for adolescent clinical patients	Until 2010	Medline	Not reported (article was narrative)	1: Monti 1999

D'Onofrio 2002 (279)	Screening and BI for alcohol problems in the ED	1996 (does not report stop date, likely 2001/02)	Medline, Cochrane Library	27	1: Monti 1999
Drake 2008 (280)	Psychosocial interventions for those with co-occurring severe mental illness and substance use disorder.	Not reported. Report submitted in Aug 2006.	ACP Journal Club, Bandolier, BMJ Updates, Clinical Evidence, Cochrane Database of Systematic Reviews, Evidence-Based Mental Health, Medline/PubMed, Project CORK, PsycINFO, TRIP Database Plus, several journals (Psychiatric Services, American Journal of Psychiatry, Community Mental Health Journal, Journal of Nervous and Mental Disease, and Journal of Substance Abuse Treatment), and "queried staff at U.S. federal health care agencies to identify studies".	45	None
Elliot 2005 (281)	Secondary interventions for young drug users.	1990-2001	ASSIA, BIDS, Caredata, Cochrane Library, DARE, Department of Health Technology Assessment Database (UK), Health Development Agency (UK), Drug and Alcohol findings (UK), Health Education Board for Scotland (HEBS), Medline, MIMAS Web of Science, National Research Register (UK), NHS Centre for Reviews Dissemination, National Institute on Drug Abuse (NIDA; USA).	7 reviews and 9 original study articles	None
Foxcroft 2002 (282)	Summarize rigorous evaluations of psychosocial and educational interventions aimed at the primary prevention of alcohol misuse by young people.	Until 2002	ASSIA, BIDS, CORK, DRUG-database, DRUG-INFO, EMBASE, ERIC, ETOH, FAMILY-RESOURCES DATABASE, HEALTH-PERIODICALS-DATABASE, MEDLINE, PSYCLIT, SIGLE, SOMED, and greay literature including Dissertation-Abstracts, Social-Work-Abstracts, National-Clearinghouse-on-Alcohol-and-Drug-Information, Mental-Health-Abstracts	20	1: Monti 1999
Guillemont 2013 (283)	Interventions to prevent alcohol use among children and adolescents	2007 to Feb 2012	Cochrane, PubMed, Trip, and reference lists of NICE guidelines	27	None

Hamm 2010 (284)	ED-based management interventions for mental health presentations	1985-2009	MEDLINE®, Ovid MEDLINE® In-Process & Other Non-Indexed Citations, EMBASE, Cochrane Central Register of Controlled Trials, OVID HealthStar, Cochrane Database of Systematic Reviews, Health Technology Assessment Database, Database of Abstracts of Reviews of Effects, ACP Journal Club, PsycINFO®, CINAHL®, SocIndex, ProQuest Theses and Dissertations, and Child Welfare Information Gateway. ClinicalTrials.gov, reference lists, key journals, and conference proceedings (Canadian Association of Emergency Physicians, Society for Academic Emergency Medicine, American College of Emergency Physicians, Canadian Paediatric Society).	12	None
Havard 2008 (285)	ED-based interventions for alcohol use	January 1996-July 2007	ACP Journal Club, CCTR, CDSR, DARE, EMBASE, Global Health, Ovid MEDLINE®, PsycINFO, SWAB, Current Contents Connect and Web of Science	13	3: Maio 1995, Monti 1999, Spirito 2004
Jackson 2012 (286)	Interventions for preventing substance use and risky sexual behaviour in young people	Until 2008	ASSIA, CINAHL, Cochrane Methodology Register, Cochrane Database of Systematic Reviews, DARE, Department of Health Reviews Database, EMBASE, Medline, NHS EED, PsycINFO, Social Science Citation Index via Web of Science, and key journals (Alcoholism: clinical and experimental research, British Medical Journal, Addiction, Archives of Internal Medicine, Academic Emergency Medicine, Worldviews on Evidence Based Nursing, Journal of Clinical Nursing, Alcohol Drug and Alcohol Dependence, Preventative Medicine, Annals of Internal Medicine, Journal of General Internal Medicine)	27	3: Maio 1995, Monti 1999, Spirito 2004
Jenkins 2009 (287)	Interventions to reduce alcohol consumption	1995-2005	CINAHL, EMBASE, Medline, PsycINFO	44 of 42 distinct studies	1: Monti 1999
Lundahl 2013 (288)	Motivational interventions within medical care settings	1983 to Aug 2011	CINAHL, Health Source: Nursing/Academic Edition, MedLine, Motivational Interviewing Network of Trainers bibliography PsycARTICLES, PsycINFO, PubMed, Scopus, Social Work Abstracts, Web of Knowledge	48	1: Bernstein 2009, Johnston 2002

Nilsen 2008 (289)	Hospital-based BIs to reduce alcohol use in injured patients	Until January 2007	Medline, PsychLIT, CINAHL, and the Cochrane Library, and hand searches of specialist alcohol, injury prevention, and emergency care journals.	14	1: Maio 2005
Patton 2014 (290)	Alcohol screening and BIs for adolescents.	2003-2013	PubMed, Web of Science	Not reported (article was narrative)	1: Walton 2010
Spoth 2007(291)	Interventions targeting alcohol use in youth	Not reported, but will be before (and possibly including) 2007	Does not describe search fully. Does mention that search included Science Citation Index Expanded, PsycINFO, Medline, and the Social Science Citation Index, and 'additional relevant book and book chapters', and 'relevant internet sources'.	13 distinct programmes in 10-15 year olds, 3 in 16+ year olds	None
Steinka-Fry 2015 (292)	BIs on drink driving outcomes among youth	Until Dec 2012	CINAHL, Clinical Trials Register, Dissertation Abstracts International, ERIC, International Bibliography of the Social Sciences, NIH RePORTER, PsycARTICLES, PsycINFO, PubMed, Social Services Abstracts, Sociological Abstracts, and WorldWideScience.org, and grey literature searching, including websites, conference proceedings, hand searching of journals, and harvesting of references from bibliographies.	30 of 12 distinct studies	2: Maio 2005, Spirito 2004
Tait 2003 (293)	BIs in reducing alcohol, tobacco or other drug use among adolescents	Until 2002	MEDLINE, PsychINFO, Current Contents, Cochrane Database of Systematic Reviews, Sociological Abstracts and AustHealth (including the DRUG and CINCH-Health databases), and the CD version of EMBASE (Pharmacology and Drugs 1993 – 1998).	11	1: Monti 1999
Tait 2013 (294)	Internet-based interventions in decreasing the frequency of cannabis use	Until Sep 2012 (update of Tait 2003 (293))	EMBASE, Medline, PsycINFO, Pubmed,	10	None

Tait 2015 (295)	Computer-based or online interventions to reduce alcohol consumption, sexual assault, and intimate partner violence	Jun 2003-Jan 2015	CINAHl, EMBASE, Global Health, Medline, ProQuest, PsycINFO, Pubmed,	5 of 4 distinct studies	1: Cunningham 2012
Tanner-Smith 2015a (296)	BIs to reduce alcohol use among adolescents (age 11–18) and young adults (age 19–30)	Until Dec 2012	CINAHL, Clinical Trials Register, Dissertation Abstracts International, ERIC, International Bibliography of the Social Sciences, NIH RePORTER, PsycARTICLES, PsycINFO, PubMed, Social Services Abstracts, Sociological Abstracts, WorldWideScience.org, several additional grey literature sources (e.g., Australasian Medical Index, Google Scholar), conference proceedings (see Tanner-Smith and Lipsey 2014 for complete details).	313 for 185 distinct studies	Individual studies were not referenced.
Tanner-Smith 2015b (297)	As Tanner-Smith 2015a, but looked at outcomes of concurrent drug use	Until Dec 2012	CINAHL, Clinical Trials Register, Dissertation Abstracts International, ERIC, International Bibliography of the Social Sciences, NIH RePORTER, PsycARTICLES, PsycINFO, PubMed, Social Services Abstracts, Sociological Abstracts, WorldWideScience.org, several additional grey literature sources (e.g., Australasian Medical Index, Google Scholar), conference proceedings (see Tanner-Smith and Lipsey 2014 for complete details).	67 of 30 distinct studies	Individual studies were not referenced.
Thomas 2013 (298)	Mentoring interventions to prevent or reduce drug/alcohol use among adolescents (update of a Cochrane review carried out by authors in 2011).	Until Jan 2013	CINAHL, the Cochrane Library, EMBASE, Eric, Medline, PsycINFO, Social Sciences Abstracts, Sociological Abstracts, ClinicalTrials.gov	6	None
Wachtel 2010 (299)	BIs in adolescents with alcohol misuse or binge drinking	Until October 2008	CINAHL, Medline, Ovid full text, Ovid, PsycINFO and Cochrane, and journals: sychology of Addictive Behaviour, Journal of Consulting and Clinical Psychology, Addictive Behaviours, The American Journal of Drug and Alcohol Abuse and Psychology of Addictive Behaviours.	14	3: Maio 2005, Monti 1999, Spirito 2004

Watson 2013 (300)	Hospital-based interventions to reduce drug/alcohol misuse	Until Aug 2011	C2-SPECTR, CINAHL, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Conference Proceedings Citation Index – Science, DARE, EMBASE, HMIC, HTA Database, Medline, NHS Economic Evaluations Database, PsycINFO, Public Health Interventions Cost Effectiveness Database.	6	None

BI = Brief intervention, ED = Emergency department

*As not specifically in adolescents who present to hospital with adversity.

C. Cleaning and coding the HES-ONS extract

C.1 Data cleaning procedure

Duplicates

I removed any records where the individual's HES ID, start and end dates, diagnoses, procedures matched.

Admission start and end dates

I defined each admission based on date variables, which gave exact dates (to the day) of when individuals were admitted, seen by different consultants, and discharged.

In the HES-ONS extract, start and end dates of admissions and of their constituent episodes were sometimes unfeasible and were clearly errors, e.g., the end date occurred before the start date. Therefore, I defined rules for dealing with date variables such that individual admissions could be logically identified:

- Where the start date of the first episode of an admission was earlier than the start date of the admission itself, this episode start date was used to re-define the admission's start date.
- If an episode's end date was later than the end date of its admission; this episode end date was used to re-define the end date.
- If an episode's or admission's start date occurred after the end date, these two dates were switched around. These 'new' dates were only retained if the start date of the new admission occurred after the end date of any previous admission, and if the end date of the new admission occurred before the start date of any following admission: if

this was not the case the original start date was retained and the end date was replaced as ‘missing’.

I removed any episodes where the start date occurred after 31st March 2012. For any end dates which occurred after this date, I changed the end date to 31st March 2012.

Dates of birth and age

The month, but not the exact day, of birth was provided in the HES-ONS extract, per individual. I assumed that the date of birth was on the 15th of the provided month (14th for those in February). Age in the HES-ONS extract was given in years, except for infants where it was given as: < 1 day, 1 to 6 days, 7 to 28 days, 29 to 90 days, 91 to 181 days, 182 to 272 days, 273 to 364 days (155) (variable ‘startage’). I defined the following rules:

- For individuals where an admission’s start or end date occurred before their assumed date of birth, their assumed date of birth was replaced with the earliest admission’s start date.
- For infants with age values of < 1 day or 1 to 6 days, their date of birth was assumed to be the same start date as the admission, or 3 days before the admission, respectively (for those with both values recorded between multiple admissions, the start date of the admission where the infant was < 1 day old took priority). Infants with other age values did not have their assumed dates of birth altered from those above.

Time-to-event data

After defining an index emergency admission for injury, and calculating times from discharge to death and re-admission, the following rules applied:

- For any calculated times (since 1 day after discharge from the index admission) that were negative, these times and start and end dates of both the index admission and date of death or re-admission, were eyeballed manually.
- For those individuals where the time was close to -365 days, it was assumed that the year of death or re-admission had been entered wrongly, and was replaced with the year + 1.
- For all other deaths or re-admissions that were negative, these events were labelled as censored, and the date was replaced with the end date of the index admission.

C.2 ICD-10 coding clusters for violence, self-harm, drug/alcohol-misuse and accidents

Clusters and descriptions*	ICD-10 codes
Violence	
Maltreatment-related	
Maltreatment syndromes	T74
Effects of other deprivation (extreme neglect)	T73
Perpetrator of neglect and other maltreatment syndromes	Y06, Y07
Assault	
Assault by bodily force and sexual assault	Y04, Y05
Other types of assault	X85 - Y03, Y08 - Y09
Undetermined cause	
Events of undetermined intent	Y20 - Y34
Examination and observation following other inflicted injury	Z04.5
Examination and observation for other reasons: request for expert evidence	Z04.8
Adverse social circumstances	
~~Neonatal withdrawal symptoms from maternal use of drugs of addiction~~	~~P96.1~~
~~Other problems related to physical environment~~	~~Z58.8~~
~~Problem related to physical environment, unspecified~~	~~Z58.9~~
~~Homelessness~~	~~Z59.0~~
~~Inadequate housing~~	~~Z59.1~~
~~Lack of adequate food~~	~~Z59.4~~
~~Extreme poverty~~	~~Z59.5~~
~~Insufficient social insurance and welfare support~~	~~Z59.7~~
~~Problem related to housing and economic circumstances, unspecified~~	~~Z59.9~~
~~Problems related to social environment~~	~~Z60~~
~~Problems related to negative life events in childhood~~	~~Z61~~
~~Other problems related to upbringing~~	~~Z62~~
~~Other problems related to primary support group~~	~~Z63~~
~~Discord with counsellors~~	~~Z64.4~~
~~Problems related to other legal circumstances~~	~~Z65.3~~
~~Other specified problems related to psychosocial circumstances~~	~~Z65.8~~
~~Problem related to unspecified psychosocial circumstances~~	~~Z65.9~~
~~Problems related to lifestyle~~	~~Z72.3 - Z72.9~~
~~Problems related to care-provider dependency~~	~~Z74~~

~~Health supervision and care of foundling~~	~~Z76.1~~
~~Health supervision and care of other healthy infant and child~~	~~Z76.2~~
~~Family history of mental and behavioural disorders~~	~~Z81~~
~~Personal history of other specified risk-factors, not elsewhere classified~~	~~Z91.8~~

Self-harm	
Intentional self-poisoning by and exposure to…	
…drugs	X60-X63
…other and unspecified drugs, medicaments and biological substances	X64
…alcohol	X65
…organic solvents and halogenated hydrocarbons and their vapours	X66
…other gases and vapours	X67
…pesticides	X68
…other and unspecified chemicals and noxious substances	X69
Intentional self-harm by…	
…hanging, strangulation and suffocation	X70
…drowning and submersion	X71
…firearm discharge	X72-X74
…explosive material	X75
…smoke, fire and flames, or steam, hot vapours and hot objects	X76-X77
…sharp/blunt objects	X78-X79
…jumping from a high place	X80
…jumping or lying before a moving object, or crashing a motor vehicle	X81-82
…other specified means	X83
…unspecified means	X84
Personal history of self-harm	Z91.5
Sequelae of intentional self-harm	Y87.0

Drug or alcohol misuse	
Drugs, medicaments and biological substances (illicit drugs)	
Mental and behavioural disorders due to psychoactive substance use	F11 - F17, F19
Drug-induced myopathy	G72.0
Drug-induced acute pancreatitis	K85.3

Finding of drugs not normally found in blood	R78.1 - R78.5
Poisoning by drugs, medicaments and biological substances	T36 - T50 (not including T50.6)
Poisoning, undetermined intent	Y10 - Y14
Drug rehabilitation	Z50.3
Drug abuse counselling and surveillance	Z71.5
Drug use	Z72.2
Environmental/ Domestic substances	
Mental and behavioural disorders due to use of volatile solvents	F18
Accidental poisoning by and exposure to noxious substances	X40 – X44, X46 - X49
Intentional self-poisoning by and exposure to noxious substances	X69
Poisoning by chemical or noxious substance, undetermined intent	Y16 - Y19
Codes mentioning both alcohol and drugs	
Special epileptic syndromes - (related to alcohol, drugs, etc.)	G40.5
Blood-alcohol and blood-drug test	Z04.0
Alcohol	
Alcohol-induced pseudo-Cushing's syndrome	E24.4
Mental and behavioural disorders due to use of alcohol	F10
Degeneration of nervous system due to alcohol	G31.2
Alcoholic polyneuropathy	G62.1
Alcoholic myopathy	G72.1
Alcoholic cardiomyopathy	I42.6
Alcoholic gastritis	K29.2
Alcoholic liver disease	K70
Alcohol-induced acute pancreatitis	K85.2
Alcohol-induced chronic pancreatitis	K86.0
Maternal care for (suspected) damage to fetus from alcohol	O35.4
Finding of alcohol in blood	R78.0
Poisoning: antidotes and chelating agents, not elsewhere classified	T50.6
Toxic effect of alcohol	T51
Accidental poisoning by exposure to alcohol	X45
Poisoning by exposure to alcohol, undetermined intent	Y15
Evidence of alcohol involvement determined by blood alcohol level	Y90
Evidence of alcohol involvement determined by level of intoxication	Y91
Alcohol rehabilitation	Z50.2
Alcohol abuse counselling and surveillance	Z71.4
Alcohol use	Z72.1

Accidents	
Transport accidents	V01 - V99
Falls	W00 - W19
Exposure to inanimate mechanical forces	W20 - W49
Exposure to animate mechanical forces	W50 - W64
Accidental drowning and submersion	W65 - W74
Other accidental threats to breathing	W75 - W84
Exposure to electric current, radiation and extreme ambient air temperature and pressure	W85 - W99
Exposure to smoke, fire and flames	X00 - X09
Contact with heat and hot substances	X10 - X19
Contact with venomous animals and plants	X20 - X29
Exposure to forces of nature	X30 - X39
Accidental poisoning by and exposure to noxious substances	X40 - X49
Overexertion, travel and privation	X50 - X57
Accidental exposure to other and unspecified factors	X58 - X59

*Strikethrough indicates that these codes were originally included and removed after further review.

The cluster for violence was based on previous work by Gonzalez-Izquierdo *et al* (154).

C.3 ICD-9 and ICD-10 coding clusters for homicide, suicide, drug/alcohol-related deaths and accidental deaths

Clusters ICD version Descriptions	ICD-9/10 codes
Homicide	
ICD-9:	
Homicide and injury purposely inflicted by other persons	E960 - E969
ICD-10:	
Maltreatment-related	
Maltreatment syndromes	T74
Effects of other deprivation (extreme neglect)	T73
Perpetrator of neglect and other maltreatment syndromes	Y06, Y07
Assault	
Assault by bodily force and sexual assault	Y04, Y05
Other types of assault	X85 – X99, Y01 - Y09
Adjourned inquest	U50.9

Suicide	
ICD-9:	
Suicide and self-inflicted injury	E950 - E959
Injury undetermined whether accidentally or purposely inflicted	E980 - E989
ICD-10:	
Intentional self-poisoning by and exposure to…	
…drugs	X60 - X63
…other and unspecified drugs, medicaments and biological substances	X64
…alcohol	X65
…organic solvents and halogenated hydrocarbons and their vapours	X66
…other gases and vapours	X67
…pesticides	X68
…other and unspecified chemicals and noxious substances	X69
Intentional self-harm by…	
…hanging, strangulation and suffocation	X70
…drowning and submersion	X71
…firearm discharge	X72 - X74
…explosive material	X75
…smoke, fire and flames, or steam, hot vapours and hot objects	X76 - X77
…sharp/blunt objects	X78 - X79
…jumping from a high place	X80

…jumping or lying before a moving object, or crashing a motor vehicle	X81 - 82
…other specified means	X83
…unspecified means	X84
Undetermined intent	
Poisoning, undetermined intent	Y1
Hanging, strangulation and suffocation, undetermined intent	Y20
Drowning and submersion, undetermined intent	Y21
Firearm-related, undetermined intent	Y22 - Y24
Contact with explosive material, steam, hot vapours, or hot, sharp, or blunt objects, undetermined intent	Y25, Y27 - Y29
Exposure to smoke, fire and flames, undetermined intent	Y25
Falling, undetermined intent	Y30 - Y31
Crashing of motor vehicle, undetermined intent	Y32
Other or unspecified, undetermined intent	Y33 - Y34

Drug/alcohol-related death

ICD-10

Drugs, medicaments and biological substances (illicit drugs)	
Mental and behavioural disorders due to psychoactive substance use	F11 - F14, F16, F19
Finding of drugs not normally found in blood	R78.1 - R78.5
Poisoning by drugs, medicaments and biological substances	T36 - T50 (not including T50.6)
Poisoning, undetermined intent	Y10 - Y14
Drug rehabilitation	Z50.3
Drug abuse counselling and surveillance	Z71.5
Drug use	Z72.2
Environmental/ Domestic substances	
Mental and behavioural disorders due to use of volatile solvents	F18
Accidental poisoning by and exposure to noxious substances	X40 – X44, X46 - X49
Codes mentioning both alcohol and drugs	
Special epileptic syndromes - (related to alcohol, drugs, etc.)	G40.5
Blood-alcohol and blood-drug test	Z04.0
Alcohol	
Alcohol-induced pseudo-Cushing's syndrome	E24.4
Mental and behavioural disorders due to use of alcohol	F10
Degeneration of nervous system due to alcohol	G31.2
Alcoholic polyneuropathy	G62.1
Alcoholic myopathy	G72.1
Alcoholic cardiomyopathy	I42.1

Alcoholic gastritis	K29.2
Alcoholic liver disease	K70
Alcohol-induced acute pancreatitis	K85.2
Alcohol-induced chronic pancreatitis	K86.0
Maternal care for (suspected) damage to fetus from alcohol	O35.4
Finding of alcohol in blood	R78.0
Poisoning: antidotes and chelating agents, not elsewhere classified	T50.6
Toxic effect of alcohol	T51
Accidental poisoning by exposure to alcohol	X45
Poisoning by exposure to alcohol, undetermined intent	Y15
Evidence of alcohol involvement determined by blood alcohol level	Y90
Evidence of alcohol involvement determined by level of intoxication	Y91
Alcohol rehabilitation	Z50.2
Alcohol abuse counselling and surveillance	Z71.4
Alcohol use	Z72.1

Accidental

ICD-9:	
Accidents	E800 - E949
Legal intervention	E970 - E978
Injury resulting from operations of war	E990 - E999
ICD-10:	
Transport accidents	V01 - V99
Falls	W00 - W19
Exposure to inanimate mechanical forces	W20 - W49
Exposure to animate mechanical forces	W50 - W64
Accidental drowning and submersion	W65 - W74
Other accidental threats to breathing	W75 - W84
Exposure to electric current, radiation and extreme ambient air temperature and pressure	W85 - W99
Exposure to smoke, fire and flames	X00 - X09
Contact with heat and hot substances	X10 - X19
Contact with venomous animals and plants	X20 - X29
Exposure to forces of nature	X30 - X39
Overexertion, travel and privation	X50 - X57
Accidental exposure to other and unspecified factors	X58 - X59

C.4 ICD-10 coding cluster for chronic conditions

Disorder sub-group	ICD-10 codes
Mental/behavioural disorders	~~E24.4~~, F00-F01, F02.8, F03-F09, F20-F48, F50, F53, F54, F60-F69, Z86.5, F70-F79, F80.0-F80.2, F80.8, F80.9, F81-F84, F88, F89, F90-F98, ~~F10-F19~~, ~~G31.2~~, ~~G40.5~~, ~~G62.1~~, ~~G72.0~~, ~~G72.1~~, ~~I42.6~~, ~~K29.2~~, ~~K70~~, ~~K85.2~~, ~~K85.3~~, ~~K86.0~~, ~~O35.4~~, ~~X60-X84~~, ~~Y10-Y14~~, ~~Y15~~, ~~Y16-Y19~~, Y20-Y34, Y47, Y49, ~~Y87.0~~, Y87.2, ~~Z50.2, Z50.3, Z71.4, Z71.5~~, Z86.4, ~~Z91.5~~
Cancer/blood disorders	C00-C97, D00-D02, D05-D09, D12, D13, D14.1-D14.4, D15, D20, D32-D35, D37-D48, D56.0-D56.2, D56.4, D56.8, D56.9, D57.0-D57.2, D57.8, D58, D61.0, D61.9, D63.0, D66, D67, D68.0-D68.2, D68.4-D68.9, D69, D70-D76, D80-D84, E34.0, E88.3, G13.0, G13.1, G53.2, G53.3, G55.0, G63.1, G73.1, G73.2, G94.1, M36.0, M36.1, M36.2-M36.4, M49.5, M82.0, M90.4, M90.6, M90.7, N08.1, N08.2, N16.1, Q98.0, Y43.1-Y43.3, Y84.2, Z08, Z51.0-Z51.2, Z54.1, Z54.2, Z85, Z86.0, Z86.2, Z92.3
Chronic infections	A15-A19, A50, A81, B18, B20-B24, B37.1, B37.5, B37.6, B37.7, B38.1, B39.1, B40.1, B44.0, B44.7, B45, B46, B48.7, B50.0, B51.0, B52.0, B55, B57.2-B57.5, B58.0, B59, B67, B69, B73, B74, B78.7, B90-B94, B02.1, E35.0, F02.4, K23.0, K23.1, K67.3, K93.0, K93.1, M00, M01.1, M49.0, N33.0, P35.0-P35.2, P35.8, P35.9, P37.0, P37.1, R75, Z21
Respiratory	E84, G47.3, J41-J47, J60-J70, J80-J86, J96.1, J98, P27, P75, Q30-Q37, Q79.0, S17, S27, S28, T27, T91.4, Y55.6, Z43.0, Z93.0, Z94.2
Metabolic/ endocrine/ digestive/ renal/ genitourinary	D55, D63.8, E00, E03.0, E03.1, E07.1, E10-E14, E22.0, E23.0, E25, E26.8, E29.1, E31, E34.1, E34.2, E34.5, E34.8, E66, E70-E72, E74-E78, E79.1-E79.9,E80.0-E80.3, E80.5, E80.7, E83, E85, E88.0, E88.1, E88.8, E88.9, G13.2, G59.0, G63.2, G63.3, G63.8, G73.5, G73.6, G99.0, G99.8, I68.8, I79.2, K20, K21.0, K22, K23.8, K25-K28, K29.0, K29.1, K29.3-K29.9, K31, K50-K52, K55, K57, K59.2, K63.0-K63.3, K66, K72-K76, K80-K83, K85.0, K85.1, K85.8, K85.9, K86.1-K86.9, K87.0, K90, L99.0, M07.4, M07.5, M09.1, M09.2, M14.2, M14.3, M14.4, M14.5, M90.8, N00-N05, N07, N08.3, N08.4, N11-N15, N16.0, N16.2, N16.3, N16.4, N16.5, N16.8, N18, N19, N20-N23, N25, N26, N28, N29, N31, N32, N33.8, N35, N36, N39.1, N39.3, N39.4, N40-N42, N70-N74, N80-N82, N85, N86, N87,N88, O24, P96.0, Q38.0, Q38.3, Q38.4, Q38.6-Q38.8, Q39, Q40.2, Q40.3, Q40.8, Q40.9, Q41, Q42, Q43.1, Q43.3-Q43.7, Q43.9, Q44, Q45, Q50.0, Q51, Q52.0-Q52.2, Q52.4, Q54.0-Q54.3, Q54.8, Q54.9, Q55.0, Q55.5, Q56, Q60.1, Q60.2, Q60.4-Q60.6, Q61, Q62.0-Q62.6, Q62.8, Q63.0-Q63.2, Q63.8, Q63.9, Q64, Q79.2-Q79.5, Q87.8, Q89.1, Q89.2, T82.4, T83.1, T83.2, T83.4-T83.9, T85.5, T86.1, T86.4, Y42.1, Y42.3, Y60.2, Y61.2, Y62.2, Y84.1, Z43.2-Z43.4, Z46.5, Z49, Z86.3, Z90.3, Z90.4, Z93.2-Z93.5, Z93.6, Z93.8, Z94.0, Z99.2

Musculoskeletal/ skin	G55.1-G55.3, G63.5, G63.6, G73.7, J99.0, J99.1, L10, L11.0, L11.8, L11.9, L12-L14, L28, L40-L45, L57, L58.1, L59, L62.0, L87, L88, L90, L92, L95, L93, L98.5, M05, M06, M07.0-M07.3, M07.6, M08, M09.0, M09.8, M10-M13, M14.0, M14.6, M14.8, M30-M35, M40-M43, M45-M48, M50-M54, M60-M62, M63.8, M80.1-M80.9, M81.1-M81.9, M82.1, M82.8, M84.0-M84.2, M84.8, M84.9, M85, M86.3-M86.6, M89, M90.0, M91-M94, N08.5, Q18.8, Q65.0-Q65.2, Q65.8, Q65.9, Q67.5, Q68.2, Q71-Q73, Q74, Q75.3-Q75.9, Q76.1-Q76.4, Q77, Q78, Q79.6, Q79.8, Q80, Q81, Q82.0-Q82.4, Q82.9, Q86.2, Q87.0-Q87.5, Q89.4, Q89.7-Q89.9, Y45.4, Y83.5, Z89.1, Z89.2, Z89.5-Z89.8, Z97.1
Neurological	F02.2, F02.3, F80.3, G00-G09, G10-G12, G13.8, G14, G20-G23, G24.1-G24.9, G25-G30, G31.0-G31.1, G31.8, G31.9, G32-G37, G40.0-G40.4, G40.6-G40.9, G41, G43-G46, G47.0-G47.2, G47.4-G47.9, G50-G52, G53.0, G53.1, G53.8, G54, G55.8, G56-G58, G59.8, G60, G61, G62.0, G62.2-G62.9, G64, G70, G71,G72.2-G72.9, G73.0, G73.3, G80-G83, G90-G93, G94.2, G94.8, G95, G96, G98, G99.1, G99.2, H05.1-H05.9, H13.3, H17, H18, H19.3, H19.8, H21, H26, H27, H28.0-H28.2, H31, H32.8, H33, H34, H35, H40, H42.0, H43, H44, H47, H54.0-H54.2, H54.4, H60.2, H65.2-H65.4, H66.1-H66.3, H69.0, H70.1, H73.1, H74.0-H74.3, H75.0, H80, H81.0, H81.4, H83.0, H83.2, H90.0, H90.3, H90.5, H90.6, H91, I60-I67, I68.0, I68.2, I69, I72.0, I72.5, P10, P21.0, P52, P57, P90, P91.1, P91.2, P91.6, Q00-Q07, Q10.4, Q10.7, Q11-Q12, Q13.0-Q13.4, Q13.8, Q13.9, Q14-Q16, Q75.0, Q75.1, Q85, Q86.0, Q86.1, Q86.8, Q90-Q93, Q95.2, Q95.3, Q97, Q99, R56.8, T85.0, T85.1, T85.2, T85.3, Y46.0-Y46.6, Y46.7-Y46.8, Z44.2, Z45.3, Z98.2
Cardiovascular	143.1, 152.8, M03.6, N08.8, Q20-Q26, Q27, Q28, Q89.3, T82.0-T82.3, T82.5-T82.9, T86.2, Y60.5, Y61.5, Y62.5, Y84.0, Z45.0, Z50.0, Z94.1, Z95
Other/non-specific	R62, R63.3, Z43.1, Z51.5, Z75.5, Z93.1, Z99.3

*Strikethrough indicates that code already forms part of cluster of codes for adversity, and so is not included in the cluster of codes for chronic conditions
This cluster w as based on previous w ork by Hardelid *et al* (180).

D. Publications resulting from thesis

D.1 Herbert *et al*, BMJ Open 2015

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Violence, self-harm and drug or alcohol misuse in adolescents admitted to hospitals in England for injury: a retrospective cohort study

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ABSTRACT

Objectives: Of adolescents in the general population in England, we aimed to determine (1) the proportion that has an emergency admission to hospital for injury related to adversity (violence, self-harm or drug or alcohol misuse) and (2) the risk of recurrent emergency admissions for injury in adolescents admitted with adversity-related injury compared with those admitted with accident-related injury only.

Design: We used longitudinally linked administrative hospital data (Hospital Episode Statistics) to identify participants aged 10–19 years with emergency admissions for injury (including day cases lasting more than 4 h) in England in 1998–2011. We used the Office for National Statistics mid-year estimates for population denominators.

Results: Approximately 4.3% (n=141 248) of adolescents in the general population (n=3 254 046) had one or more emergency admissions for adversity-related injury (girls 4.6%, boys 4.1%), accounting for 50% of all emergency admissions for injury in girls and 29.1% in boys. Admissions for self-harm or drug or alcohol misuse commonly occurred in the same girls and boys. Recurrent emergency admissions for injury were more common in adolescents with adversity-related injury (girls 17.3%, boys 16.5%) than in those with accident-related injury only (girls 4.7%, boys 7.4%), particularly for adolescents with adversity-related injury related to multiple types of adversity (girls 21.1%, boys 24.2%).

Conclusions: Hospital-based interventions should be developed to reduce the risk of future injury in adolescents admitted for adversity-related injury.

INTRODUCTION

Many adolescents exposed to adversity such as violence, self-harm or drug or alcohol misuse use secondary health services,[1 2] often repetitively.[3 4] For example, in a self-report survey of participants aged 15–16 years in England, 12.6% of those who had self-harmed had presented to hospital.[2] It is also estimated that approximately one-third of patients attending a hospital in England for self-harm re-attend for self-harm in the following year.[4] Improved management of adolescents exposed to adversity could reduce risk of repetition as well as the burden on secondary care.[5–7]

An admission to hospital provides the 'teachable moment'.[8] That is, both adolescents and their families may be more likely to engage with an intervention than if they had received it elsewhere. Hospital-based interventions to reduce the risk of future harm could benefit these adolescents by reducing episodes of injury, and may reduce recurrent emergency (ie, acute or unplanned) admissions for injury.

To date, there is a lack of evidence on how different types of adversity-related injury occur in the same adolescents over time. In addition, policymakers and service providers need to know how many adolescents have an emergency admission to hospital for adversity-related injury, their characteristics and their specific rates of readmission if they are to be feasibly targeted for intervention.

In this study, we used administrative hospital data and the Office for National Statistics (ONS) mid-year population estimates to estimate the number of adolescents in the general

Strengths and limitations of this study

- Hospital Episode Statistics (HES) captured data on all admissions to National Health Service hospitals in England at 10–19 years of age in this study's cohort.
- The longitudinal link between admissions for each individual in HES data allowed us to study the burden of multiple emergency admissions for injury over time.
- However, violence, self-harm and drug or alcohol misuse are not always recognised at an admission, or consistently recorded, and therefore this study's estimates of prevalence of adversity are likely to be underestimates.

population who have ever had an emergency admission to hospital for injury. We then estimated the prevalence of emergency admissions for injury related to violence, self-harm and drug or alcohol misuse (alone and co-occurring) in the general population. Finally, we determined the risk of recurrent emergency admissions for injury in adolescents who had at least one admission between 10 and 19 years of age for adversity-related injury compared with adolescents only ever admitted for accidental injury during the same period.

METHODS

Study population

Using administrative data from all admissions to National Health Service hospitals in England (Hospital Episode Statistics (HES)) in 1998–2011,[9] we derived a retrospective cohort of adolescents who turned 10 years old in 1998–2002, who could be observed throughout adolescence until 19 years (see online supplementary table S1).[10] Each individual also had to have at least one emergency admission for injury between 10 and 19 years of age.

Admission data

The Health and Social Care Information Centre provided pseudonymised data on hospital admissions, the use of which did not require Research Ethics Committee approval.[11] An admission is defined by the National Health Service as any hospital case lasting longer than 4 h, and so includes long day-cases as well as overnight stays. We analysed any hospital transfers or admissions within 1 day after discharge as the same admission, as previously described.[12] We used the variable for method of admission ('admimeth') to define an emergency admission. We used all International Classification of Diseases 10th Edition (ICD-10) diagnosis codes recorded during an admission to categorise admissions as being for injury related to adversity or an accident (see online supplementary table S2).[13]

Types of injury and age at emergency admission

We defined an emergency admission for injury as being related to adversity, comprising violence (maltreatment/assault/undetermined causes of injury), self-harm, or drug or alcohol misuse, using mutually exclusive clusters of ICD-10 codes (see online supplementary table S2). Violence was defined by previously validated codes, which would trigger consideration of violence by carers, peers or strangers.[12 14 15] We defined self-harm using codes that mentioned either 'self-harm' or 'self-poisoning'. Drug or alcohol misuse was defined by codes that mentioned 'alcohol', 'drugs', 'noxious substance' or 'solvent'. We defined an injury as being related to accidents only if no adversity codes were present, but there were codes from the ICD-10 *Accidents* subchapter (V01-X59).[13]

We grouped age at each admission to reflect age of onset of puberty (10–14 years), age of sitting secondary school examinations (15–17 years) and the legal age for buying alcohol (18–19 years).[16–19]

Classification of adolescents according to types of injury and age at emergency admissions

We classed adolescents into groups according to all of their emergency admissions for injury between 10 and 19 years of age. Adolescents were classed as belonging to the 'adversity' group (any adversity-related injury between 10 and 19 years of age), 'accidents-only' group (no adversity-related injury but one or more accident-related injuries) or 'other causes' group (no adversity-related or accident-related injuries) (see online supplementary figure S1). Among adolescents in the adversity group, we determined the proportion exposed to violence-related, self-harm-related and drug or alcohol misuse-related injury at age 10–19 years, respectively. We further classified the adversity group into seven mutually exclusive subgroups: violence only, self-harm only, drug or alcohol misuse only, violence and self-harm, violence and drug or alcohol misuse, self-harm and drug or alcohol misuse, and violence, self-harm and drug or alcohol misuse.

We also grouped adolescents as above, according to their emergency admissions for injury at 10–14 years only, 15–17 years only and 18–19 years only (see online supplementary figure S2).

Population denominators

We used ONS mid-year population estimates to derive population denominators.[20 21] These data are freely available online, broken down by sex and year of age.

Analyses

We estimated the proportion of adolescents in the general population who had an emergency admission for injury between 10 and 19 years of age. We used the number of adolescents in our derived retrospective cohort as the numerator and ONS mid-year estimates for participants aged 10 years in 1998–2002 as the population denominator. We then calculated these proportions by types of injury at 10–19 years of age (adversity-related (adversity group and seven mutually exclusive subgroups) and accidents only (accidents-only group)) and by age group, as described above.

We calculated the proportion of adolescents in the adversity group (and subgroups) and in the accidents-only group who had an emergency admission for injury twice and three or more times between 10 and 19 years of age. We also calculated the proportions of adolescents with two or three or more admissions of any type (including non-emergency and non-injury).

We reported all results separately for girls and boys since differences between girls and boys have been reported for prevalence of adversity in the general population.[1 22–24] We calculated 95% CIs for all proportions but did not present them here as they were all too narrow to convey any useful information (within one unit of the sample estimate). Analyses were carried out in StataSE V.12.

RESULTS

There were 1 033 702 adolescents in HES admissions data in 1998–2011, of which 402 916 formed the study cohort (462 476 emergency admission for injury when considering multiple presentations from the same adolescent, 802 682 admissions of any type (including non-emergency and non-injury, 662 727 of which were overnight stays)) (table 1), representing 12.4% (402 916/3 254 046) of the adolescent population. Twice as many boys as girls had an emergency admission for injury during adolescence (144 158/1 588 942 girls in the population (8.7%); 258 503/1 665 104 boys (16.3%)).

Types of injury and age at emergency admission

One-third of the cohort (141 248, 4.3% of the population) had a record of an emergency admission for adversity-related injury between 10 and 19 years of age (the adversity group; 157 004 emergency admissions for adversity-related injury in total) (table 1), with similar rates between sexes (72 805, 4.6% girls in the population; 68 403, 4.1% boys).

The remaining two-thirds of the cohort (261 668, 8.1% of the adolescent population) had emergency admissions for injury which were never related to adversity (table 1). Among these adolescents, 233 907 (89.4%) had an accident-related injury (the accidents-only group, 7.2% of the population) and 27 761 (10.6%) had no accident-related injury (other causes group, 0.9% of the population). A high proportion of the other causes group were affected by a chronic condition[i] between 10 and 19 years of age (11 221/27 761, 40.4%), compared with the adversity group (45 321/141 248, 32.1%) or accidents-only group (49 434/233 907, 21.1%).

Proportions of adolescents in the general population and within individual age groups by adversity (and subgroups), accidents-only, and other causes groups are provided in online supplementary table S3.

Types of adversity-related injury

Among adolescents in the adversity group (girls 72 805, boys 68 403) (figure 1), the most common type of adversity was drug or alcohol misuse (girls 91.5%, boys 60%). A higher proportion of boys than girls were exposed to violence (girls 8.5%, boys 47.6%), but a higher proportion of girls than boys were exposed to self-harm (girls 74.6%; boys 32.9%).

Girls in the adversity group were most likely to be exposed to multiple types of adversity between 10 and 19 years of age (69.2%+2.0%+1.2%+0.2%=72.6%; figure 1), especially self-harm and drug or alcohol misuse (69.2% of the entire adversity group, ie, most of the 72.6%). Fewer boys in the adversity group were exposed to multiple types of adversity (38.4%), the most common combination also being self-harm and drug or alcohol misuse (24.8%).

For most of the adolescents who were exposed to multiple types of adversity, the combination of types was recorded at the same admission. For example, among the 130 adolescent girls who were exposed to violence and self-harm between 10 and 19 years of age (table 2), 64.6% had both violence and self-harm codes present simultaneously in at least one emergency admission for injury (violence and drug or alcohol misuse 78.8%, self-harm and drug or alcohol misuse 99.7%, violence, self-harm and drug or alcohol misuse 33.9%; boys: violence and self-harm 40.1%, violence and drug or alcohol misuse 84.1%, self-harm and drug or alcohol misuse 99.1%, violence, self-harm and drug or alcohol misuse 20.0%) (data not shown).

Emergency readmissions for injury

Adolescent girls in the adversity group (50.5% of all girls in the cohort) accounted for 50% of the total number of emergency admissions for injury coming from girls (data not shown), compared with girls in the accidents-only group (41.3% of all girls) who accounted for 36.6%. Boys in the adversity group (26.2% of all boys in the cohort) accounted for 29.1% compared with 65% contributed by boys in the accidents-only group (67.7% of all boys).

More adolescents in the adversity group were readmitted for injury (ie, had two or more emergency admissions for injury) between 10 and 19 years of age (girls 17.3%, boys 16.5%; figure 2) than in the accidents-only group (girls 4.7%; boys 7.4%). Among adolescents admitted for injuries related to multiple types of adversity (table 2), the proportion readmitted was even higher (multiple types: girls 21.1%, boys 24.2%; single type: girls 7.2%, boys 10.1%).

Similarly, a higher proportion of adolescents in the adversity group had two more admissions of any type (including non-emergency and non-injury) between 10 and 19 years of age (girls 46.2%, boys 35.2%; table 2) compared with adolescents in the accidents-only group (girls 33.4%, boys 28.5%). This proportion was even higher for adolescents in the adversity group who were admitted with multiple types of adversity (multiple types: girls 49.0%, boys 42.5%; single type: girls 38.8%, boys 25.5%).

DISCUSSION

More than 1 in 20 adolescents in England had at least one emergency admission for adversity-related injury between 10 and 19 years of age. These adolescents accounted for a third of all adolescents with emergency admissions for injury and for a disproportionate number of readmissions for injury, particularly adolescents admitted with multiple types of adversity-related injury. Targeting adolescents admitted with adversity-related

[i]Defined by ICD-10 codes (see online supplementary table S2).

Table 1 Characteristics of adolescents whose entire 10 years of adolescence (ages 10–19) occurred in 1998–2011

Characteristics	Adolescent population* Total	Adolescents with emergency admission(s) for injury between 10 and 19 years of age, n (row %) Total	Adversity	Accidents only	Other causes
All	3 254 046	402 916 (100.0)	141 248 (35.1)	233 907 (58.1)	27 761 (6.9)
Age†					
Girls (years)	1 588 942	144 158 (100.0)	72 805 (50.5)	59 528 (41.3)	11 888 (8.2)
10–14		65 208 (100.0)	23 178 (35.5)	37 388 (57.3)	4642 (7.1)
15–17		48 286 (100.0)	31 573 (65.4)	12 922 (26.8)	3791 (7.9)
18–19		30 664 (100.0)	18 054 (58.9)	9155 (29.9)	3455 (11.3)
Boys (years)	1 665 104	258 503 (100.0)	68 403 (26.5)	174 267 (67.4)	15 833 (6.1)
10–14		121 821 (100.0)	17 667 (14.5)	97 478 (80.0)	6676 (5.5)
15–17		79 223 (100.0)	25 014 (31.6)	49 345 (62.3)	4864 (6.1)
18–19		57 459 (100.0)	25 722 (44.8)	27 444 (47.8)	4293 (7.5)
Missing (sex)		255 (100.0)	40 (15.7)	175 (68.6)	40 (15.7)

*Based on the Office for National Statistics (ONS) mid-year England statistics for participants aged 10 years in 1998–2002.[20]
†At first emergency admission for injury.

injury could reduce their risk of future harm, the rate of readmissions to hospital and healthcare costs.[25]

Longitudinally linked admissions allowed us to study the entire 10 years of adolescence in 402 916 individuals. We were able to distinguish between types of adversity that co-occurred during adolescence or at the same admission, and to study readmissions. One weakness of this study was our reliance on diagnostic codes recorded in administrative data. Violence by carers, which could be coded under maltreatment, and drug or alcohol misuse have been shown to be under-recorded using ICD-10,[26 27] but false positives are rare.[15] To address under-recording, we used what we considered to be sensitive clusters of codes for adversity. Other factors related to recording or coding practices,[12 14 15 27 28] for example, new guidelines for defining maltreatment,[14] can also affect ascertainment. Owing to the relative insensitivity but good specificity of the coding clusters, some adolescents who were classified in the accidents-only group may in fact belong to the adversity group, but did not have their adversity recognised or recorded. Consequently, our prevalence estimates of admission for different types of adversity-related injury are likely to provide a lower bound for the true prevalence. Further, as adolescents exposed to adversity who attended the accident and emergency (A&E) department were not necessarily admitted, our prevalence estimates represent adolescents at the severe end of the adversity spectrum. Such analyses of A&E data are limited by the quality of these data in England (available since 2007) and the resulting problems with identifying reasons for presentation and accurately linking individuals to long-term outcomes.[29]

Our prevalence estimates of admission for injury related to individual types of adversity from the general

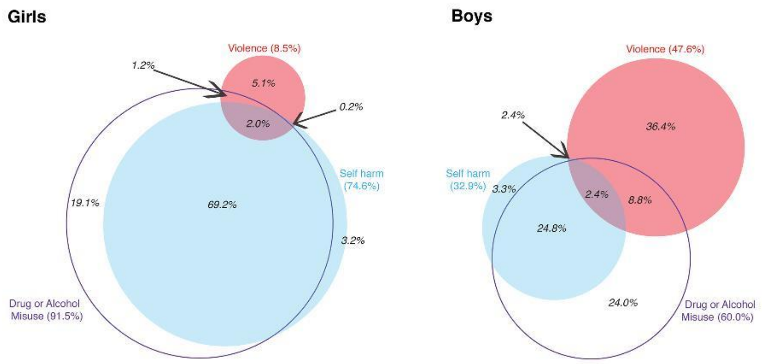

Figure 1 Number (%) of adolescents with adversity-related injury, by types of adversity between 10 and 19 years of age and sex. Each adolescent classified by all adversity recorded at any emergency admission(s) for injury between 10 and 19 years of age.

Table 2 Proportion of adolescents with 1, 2 or 3+ emergency admission(s) for injury or 1, 2 or 3+ admission(s) of any type, by types of adversity between 10 and 19 years of age*

		Girls (%)							Boys (%)						
		Emergency admission(s) for injury			Admission(s) of any type				Emergency admission(s) for injury			Admission(s) of any type			
Adolescent group*	**Number of girls**	**1**	**2**	**3+**	**1**	**2**	**3+**	**Number of boys**	**1**	**2**	**3+**	**1**	**2**	**3+**	
All	144 158	88.6	8.3	3.1	57.6	20.5	22.0	258 503	90.3	8.0	1.8	68.5	18.7	12.9	
Adversity	72 805	82.7	12.0	5.3	53.8	21.1	25.1	68 403	83.5	12.4	4.1	64.8	19.4	15.8	
Any violence	6211	77.2	13.9	8.9	49.1	20.7	30.1	32 799	83.2	12.8	4.0	65.6	19.6	14.8	
Any self-harm	54 315	79.3	13.9	6.8	51.2	21.5	27.3	21 087	76.7	15.8	7.5	57.0	20.7	22.3	
Any drug or alcohol misuse	66 645	81.9	12.5	5.6	53.6	21.1	25.3	41 014	81.1	13.6	5.3	62.9	19.5	17.6	
Single adversity	19 924	92.8	6.2	1.0	61.2	19.8	19.0	43 563	71.3	8.3	1.8	55.8	15.2	10.3	
Violence only	3734	92.4	6.3	1.3	58.1	20.4	21.6	24 912	87.1	10.6	2.2	68.3	19.2	12.6	
Self-harm only	2296	90.3	8.1	1.6	54.4	20.7	24.9	2260	87.3	10.4	2.3	62.3	19.8	17.9	
Drug or alcohol misuse only	13 894	93.3	5.9	0.8	63.2	19.5	17.4	16 391	88.5	9.5	2.1	69.9	17.9	12.2	
Multiple adversity	52 881	78.9	14.2	6.9	51.0	21.6	27.4	24 840	77.3	16.7	7.5	59.0	21.0	21.5	
V+SH	130	70.0	20.8	9.2	42.3	26.2	31.5	217	41.6	15.4	6.1	32.8	16.0	14.2	
V+DA	862	81.9	15.1	3.0	52.2	22.9	24.9	6013	84.6	17.5	5.4	68.4	21.8	17.3	
SH+DA	50 404	80.1	13.7	6.3	51.8	21.6	26.6	16 953	86.7	16.4	6.9	64.6	22.7	22.9	
V+SH+DA	1485	36.8	31.6	31.5	25.5	19.9	54.5	1657	22.0	16.4	14.1	17.9	11.7	22.8	
No adversity	71 353	94.7	4.5	0.8	61.4	19.9	18.7	190 100	92.4	6.3	0.9	69.5	18.3	11.8	
Accidents only	59 465	95.3	4.1	0.6	66.5	18.7	14.7	174 267	92.3	6.5	0.9	71.1	18.0	10.5	
Other causes	11 888	91.5	6.3	2.1	35.5	25.8	38.8	15 833	93.4	5.0	1.6	51.5	22.1	26.3	

*Each adolescent classified by all adversity/accidents seen at any emergency admission(s) for injury between 10 and 19 years of age.
DA, drug or alcohol misuse; SH, self-harm; V, violence.

adolescent population are consistent with previous reports for emergency admissions for assault-related injury in 2004–2009 and for all admissions (emergency and non-emergency) for self-harm and drug or alcohol misuse.[1 2 24 30] Previous studies have reported higher rates of drug or alcohol misuse in boys than in girls in the general adolescent population.[24] We found higher rates in girls. This difference could indicate that girls exposed to drug or alcohol misuse are more likely to be injured, to present to hospital, or to be admitted after a hospital presentation, than boys.

Our estimated rates of readmission of any type (including non-emergency and non-injury) for violence (girls 50.8%, boys 34.4%) (table 2) and self-harm (girls 48.8%, boys 43.0%) were higher than previously reported (11% for violence, 33% for self-harm).[3 4]

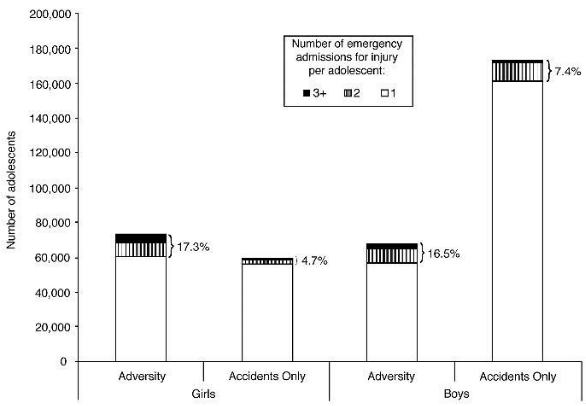

Figure 2 Number of adolescents with 1, 2 and 3 or more emergency admission(s) for injury between 10 and 19 years of age, by types of injury between 10 and 19 years of age and sex. Percentages are of adolescents who have two or more emergency admissions for injury between 10 and 19 years of age. Each adolescent was classified by all adversity/accidents recorded at any emergency admission(s) for injury.

These discrepancies are likely because we considered the whole 10 years of adolescence and readmission of any type, whereas previous studies looked at re-attendance up to the following year and for the same type of adversity-related injury.[3 4]

The results of this study should inform policy initiatives and national guidelines. First, a substantial proportion of adolescents are affected by adversity and they account for a large proportion (29.1–50.0%) of all emergency admissions to hospital for injury in this age group. Second, we show the large burden of injury admission for all three types of adversity, yet there are currently no national clinical guidelines for managing cases of violence, other than responding to violence by caregivers.[31] Finally, these results show that adolescents often present with multiple types of adversity (especially in girls), even though guidelines exist only for managing individual problems.[32–34]

In addition, policymakers need to be aware of the widely varying aetiological pathways to admission with adversity-related injury. Our approach to defining this group of adolescents is not designed to reflect the complexity or severity of these cases. For example, admission for multiple types of adversity-related injury is a poor proxy indicator of severity. Effective interventions will need to be tailored to the individual based on specialist clinical assessment. However, all three types of adversity are likely to reflect a combination of underlying psychosocial need and environmental and social stressors.[35]

Hospital interventions may reduce the risk of future harm, including the incidence of other types of harm not seen in hospital, for example, further adversity-related injury not leading to admission. Further research using linked data from healthcare sectors such as A&E could shed light on the overall burden of adversity-related injury on hospitals. Although these data have limited quality in England, longitudinally linked data sets in other countries could provide insights into long-term outcomes for this vulnerable group of adolescents.

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Contributors AH conceived and designed the study, analysed and interpreted the data, drafted the article, revised it critically for important intellectual content and approved the final version to be published. LL conceived and designed the study, interpreted the data, revised the article critically for important intellectual content and approved the final version to be published. AG-I and RG conceived and designed the study, acquired and interpreted the data, revised the article critically for important intellectual content and approved the final version to be published.

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Competing interests None.

Ethics approval Both Hospital Episode Statistics (HES) admissions data and Office for National Statistics (ONS) mid-year population estimates are derived from routinely collected administrative data. HES data were pseudonymised before we received them, and therefore we did not require Research Ethics Committee approval.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data on HES are available. ONS mid-year population estimates may be accessed freely online: http://www.ons.gov.uk/ons/publications/all-releases.html?definition=tcm%3A77-22371

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RESEARCH ARTICLE

10-y Risks of Death and Emergency Re-admission in Adolescents Hospitalised with Violent, Drug- or Alcohol-Related, or Self-Inflicted Injury: A Population-Based Cohort Study

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Data Availability Statement: Extracts of Hospital Episode Statistics inpatient data linked to Office for National Statistics Mortality data can be applied for via the UK Health and Social Care Information Centre. Those requesting an extract of the data 'must clearly demonstrate that the request is being made to support the provision of health and social care and the promotion of health'.[51] Data 'cannot be released for solely commercial purposes'. More information about application, approval, and access can be found on www.hscic.gov.uk/dars. Specific requirements may

Abstract

Background

Hospitalisation for adversity-related injury (violent, drug/alcohol-related, or self-inflicted injury) has been described as a "teachable moment", when intervention may reduce risks of further harm. Which adolescents are likely to benefit most from intervention strongly depends on their long-term risks of harm. We compared 10-y risks of mortality and re-admission after adversity-related injury with risks after accident-related injury.

Methods and Findings

We analysed National Health Service admissions data for England (1 April 1997–31 March 2012) for 10–19 y olds with emergency admissions for adversity-related injury (violent, drug/alcohol-related, or self-inflicted injury; n = 333,009) or for accident-related injury (n = 649,818). We used Kaplan–Meier estimates and Cox regression to estimate and compare 10-y post-discharge risks of death and emergency re-admission. Among adolescents discharged after adversity-related injury, one in 137 girls and one in 64 boys died within 10 y, and 54.2% of girls and 40.5% of boys had an emergency re-admission, with rates being highest for 18–19 y olds. Risks of death were higher than in adolescents discharged after accident-related injury (girls: age-adjusted hazard ratio 1.61, 95% CI 1.43–1.82; boys: 2.13, 95% CI 1.98–2.29), as were risks of re-admission (girls: 1.76, 95% CI 1.74–1.79; boys: 1.41, 95% CI 1.39–1.43). Risks of death and re-admission were increased after all combinations of violent, drug/alcohol-related, and self-inflicted injury, but particularly after any drug/alcohol-related or self-inflicted injury (i.e., with/without violent injury), for which age-adjusted hazard ratios for death in boys ranged from 1.67 to 5.35, compared with 1.25 following

be discussed via email (enquiries@hscic.gov.uk). Life-table data for England are available from: www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-365199.

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Competing Interests: The authors have declared that no competing interests exist.

Abbreviations: CI, confidence interval; HES, Hospital Episode Statistics; HR, hazard ratio; HSCIC, Health and Social Care Information Centre; ICD-10, International Classification of Diseases–10th Revision; IMD, Index of Multiple Deprivation; NHS, National Health Service.

violent injury alone (girls: 1.09 to 3.25, compared with 1.27). The main limitation of the study was under-recording of adversity-related injuries and misclassification of these cases as accident-related injuries. This misclassification would attenuate the relative risks of death and re-admission for adversity-related compared with accident-related injury.

Conclusions

Adolescents discharged after an admission for violent, drug/alcohol-related, or self-inflicted injury have increased risks of subsequent harm up to a decade later. Introduction of preventive strategies for reducing subsequent harm after admission should be considered for all types of adversity-related injury, particularly for older adolescents.

Introduction

Adolescents (10–19 y olds) are a vulnerable population [1]. Community surveys of adolescents in high-income countries have estimated that up to 50%–60% are exposed to violence, drug/alcohol misuse, or self-harm [2–4]. These adverse experiences are associated with underlying psychosocial difficulties [1] and tend to co-occur [5]. There is evidence that interventions that address psychosocial difficulties have the potential to improve health and social outcomes throughout the rest of the life course [1,6,7].

A presentation to hospital for injury related to violence, drug/alcohol misuse, or self-harm provides an opportunity to assess adolescents' psychosocial needs or initiate interventions, at a time when these individuals may be willing to consider behaviour change [8–10]. Currently, national guidance in England mandates psychosocial assessment after hospital presentations for self-harm but not after presentations for violent or drug/alcohol-related injury [11]. National guidance for managing patients with violent injury does not exist, and guidelines for managing patients with drug/alcohol-related injury focus on adult patients with drug/alcohol dependence [12,13]. If adolescents presenting with these injuries are at increased risks of future harm, then psychosocial management might be appropriate.

We have previously reported the prevalence of emergency admissions for violent, drug/alcohol-related, and self-inflicted injury for adolescents in England. Approximately 4% of girls and boys have such an admission at least once between the ages of 10 and 19 y old, accounting for one-third of adolescents admitted with any injury (the majority of the remaining two-thirds are related to accidents) [5]. In England, it is estimated that among adolescents who present to hospital with self-inflicted injury, 27.3% re-present with another self-inflicted injury in the next 1–7 y [14], and at least 9.9/1,000 die in the next 1–10 y. In a recent US study of young people presenting with violent and/or drug/alcohol-related injury, 22.4%–36.7% of those surveyed within the 2 y after discharge had re-presented with a violent injury [15]. We found no published studies reporting risks of death or re-admission through any cause following all three types of adversity-related injury (violent, drug/alcohol-related, or self-inflicted injury).

We used national hospitalisation data for England to determine the cumulative risks of death and emergency re-admission in adolescents over the 10 y after discharge following an admission for violent, drug/alcohol-related, or self-inflicted injury. We determined whether risks after adversity-related injury were increased compared with after accident-related injury (our hypothesis was that they would be). We also examined whether risks of death or emergency re-admission differed by sex and age or were associated with underlying chronic conditions, ethnicity, or deprivation.

Methods

Study Design and Setting

We used anonymised Hospital Episode Statistics (HES) data comprising all hospital admissions to the National Health Service (NHS) in England from 1 April 1997 to 31 March 2012 [16]. We compared outcomes for adolescents admitted to the emergency department for an adversity-related injury with those admitted with an accident-related injury. HES data captured the vast majority of our population of interest, i.e., patients admitted to hospital for injury in England [17]. Therefore, we did not carry out a sample size calculation.

We identified adolescents (aged 10–19 y inclusive) who had one or more emergency (acute, unplanned) admissions for injury. We considered any multiple admissions within 1 d of each other, or relating to a hospital transfer, to be the same admission. We defined "emergency" admissions by the HES "method of admission" variable [18], and "injury" by the use of any "S" or "T" International Classification of Diseases–10th Revision (ICD-10) diagnosis code in the admission record [19]. Most adolescents (89%) had only one emergency admission for injury at age 10–19 y and between 1 April 1997 and 31 March 2012, which was defined as the index admission. For adolescents who had two or more emergency admissions for injury, we randomly selected one as the index admission. We chose to select an index admission randomly rather than using the first admission as this would better represent presentations seen in practice. Adolescents who died at the index admission, had an invalid discharge date, or were not discharged by 31 March 2012 were excluded from analyses.

We received a standard, de-identified data extract from the Health and Social Care Information Centre (HSCIC), which does not require research ethics approval or patient consent [20]. The original study design and analysis plan (at the outset of the study) and deviations from this plan are summarised in S1 Table.

Exposure and Outcome

We used ICD-10 codes recorded in the index admission record to define two cohorts of adolescents who were alive at discharge (Fig 1). We defined one cohort of adolescents whose index admission was for "adversity-related injury", i.e., codes indicating any injury coupled with violence, intentional self-harm, or drug/alcohol misuse We defined drug/alcohol "misuse" as any codes indicating drug or alcohol use, since emergency admission for injury combined with drug or alcohol use indicates clinically important evidence of harm. The comparison cohort comprised adolescents whose index admission record had no codes indicating adversity-related injury but codes indicating "accident-related injury". Codes used to define adversity and accidents are described elsewhere [5] and have been validated using hospital clinician records [21]. An admission may be categorised as being for more than one type of adversity-related injury because up to 20 ICD-10 codes can be recorded per admission. Adolescents who had an emergency admission for injury with no codes for adversity or accident were excluded from the analyses. The majority of those excluded had complex conditions or complications of surgery [5].

The outcomes were death and emergency re-admission at least 1 d after discharge from the index admission and up to 10 y later. Death was captured by linking hospital admissions to UK death registration data from the Office for National Statistics [22]. Re-admissions were captured by linking records for the same person using a HES pseudo-identifier, which was specific to our data extract. These identifiers are generated by the HSCIC using a deterministic algorithm to link all episodes of care within the English NHS using sex, date of birth, NHS number, and postcode [23]. Linkages are carried out by the HSCIC before sending out standardised data extracts.

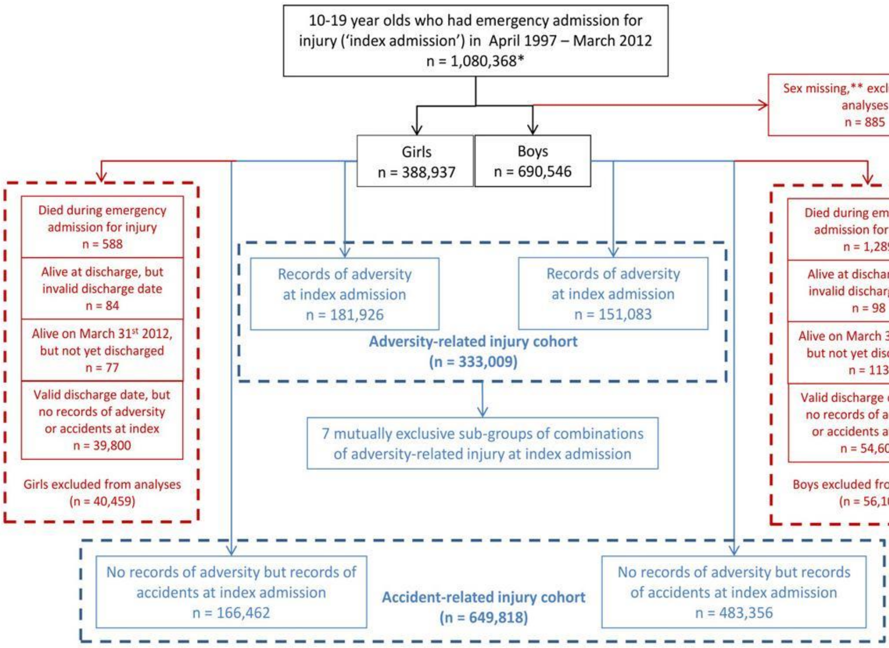

Fig 1. Formation of adversity-related injury and accident-related injury cohorts among 10–19 y olds. *49,784 girls and 80,205 boys had more than one emergency admission for injury between 10 and 19 y. For each of these adolescents, one emergency admission for injury was randomly selected as the index emergency admission for injury. **Not possible to impute any missing values at 0–30 y old.

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Confounders and Risk Factors

We included age, chronic condition status, deprivation (socioeconomic status), and ethnicity, as recorded at the index admission, as possible confounding variables, or independent risk factors, for death and re-admission, based on previous studies that have shown associations between these factors and harm in adolescents [5,24]. Other factors, such as family and neighbourhood factors, are associated with risks of future harm [25]. We did not include these confounding factors in our analyses as they are unlikely to be used by clinicians or service providers to identify groups at high risk of subsequent harm who might benefit from interventions.

We grouped adolescents into three age groups (10–14, 15–17, 18–19 y) to reflect stages of development [5]. We defined a chronic condition as any record of a chronic physical or mental condition at the index or any preceding admission based on a previously validated cluster of ICD-10 codes (excluding codes for adversity) [5]. This cluster defines a chronic condition as one requiring at least 1 y of medical treatment or follow-up [26]. We grouped the 16 ethnicity categories provided in HES into five categories (white, black, Asian, mixed, other) [27], such that groups would be large enough to stratify analyses by age and sex. Deprivation was grouped according to quintiles of Index of Multiple Deprivation (IMD) score based on residential postcode (with the least deprived areas having a score lower than the first quintile and the most deprived areas having a score higher than the fourth quintile) [18,28]. We grouped deprivation by quintile because previous research has shown differences between quintiles in the incidence of admission for violent injury [29].

We addressed data quality by replacing missing or inconsistent variables with the corresponding modal value for all admission records on the same individual. We replaced 0.8% of records with modal values for sex, 30.2% for ethnicity, and 1.8% for deprivation value. We analysed any residual missing variables for sex, ethnicity, or deprivation as "missing". No data were missing for age or chronic condition status.

Analyses

All analyses were carried out separately for girls and boys, given well-established differences in the frequency of adversity-related injury between the sexes [5]. We used time-to-event analysis methods (Kaplan–Meier estimates and Cox regression) to account for variation in the length of follow-up.

To determine the absolute risks of death and emergency re-admission in each cohort, we calculated Kaplan–Meier cumulative probabilities and 95% confidence intervals (CIs) for each age group from 1 d to 10 y after discharge from the index admission. We also calculated 1-, 5-, and 10-y risks of death and re-admission following any violent, any drug/alcohol-related, and any self-inflicted injury. To allow comparison of the risks of death in the adversity-related and accident-related injury cohorts with those in the general population, we derived general population estimates of risks of death in 10–19 y olds in 1997–1999 for the next 1–10 y in 1-y increments using aggregate statistics published by the Office for National Statistics (see S2 Table for details on how these numbers were derived) [30]. A comparison of risks of re-admission in our cohorts with risks for adolescents in the general population was not possible as only 12% of the general population of adolescents had an emergency admission for injury at all [5].

We tested for differences in risks of death and emergency re-admission over time between the two cohorts using Cox regression, and present hazard ratios (HRs) with 95% CIs. Models were adjusted for confounders in stages. We first estimated crude HRs between the two cohorts, and then estimated HRs adjusting for age; age and chronic condition status; and age, chronic condition status, ethnicity, and deprivation. Estimated HRs were attenuated after adjusting for age, (e.g., by 15.5% for death in girls). However, further adjustments for chronic condition status, ethnicity, and deprivation did not substantially alter age-adjusted HRs. We therefore present the main comparison of the two cohorts adjusted by age only. However, because chronic condition status and deprivation were independently associated with death and re-admission, we report the absolute 10-y risks of these outcomes after adversity-related and accident-related injury in Table A6 in S1 Text.

As different types of adversity-related injury tend to co-occur [5], we estimated age-adjusted HRs of death and emergency re-admission for seven mutually exclusive combinations of violent, drug/alcohol-related, and self-inflicted injury (all versus accident-related injury). To determine whether there were additional risks of multiple emergency re-admissions for adolescents with adversity-related injury, we also estimated age-adjusted HRs of a second, third, fourth, and fifth emergency re-admission (less than 5% of adolescents had more than five re-admissions).

We tested the goodness of fit of the Cox regression models by plotting the Nelson–Aalen estimate of the cumulative hazard function against Cox–Snell residuals [31]. Analyses were conducted in Stata/SE 12 (StataCorp).

Results

Study Population

Of the 1,080,368 adolescents who had an emergency admission for injury, nearly one-third (n = 333,009) formed the adversity-related injury cohort, and 60% (n = 649,818) formed the accident-related injury cohort (Fig 1). The remaining 9% were excluded (0.2% who died at the index admission, 0.04% who either had an invalid discharge date or were not discharged by 31 March 2012, and 8.7% who were admitted with other causes of injury).

There were similar numbers of girls and boys in the adversity-related injury cohort, but boys outnumbered girls by 2:1 in the accident-related injury cohort (girls: 166,462, boys: 483,356). Compared with the accident-related injury cohort, adolescents in the adversity-related injury cohort were on average older at their index admission, more likely to have a chronic condition, and more likely to be from the most deprived areas according to IMD score (Table 1). The most common chronic conditions were chronic respiratory disorders (e.g., asthma), affecting 39.8% to 55.4% of the girls and boys with either adversity- or accident-related injury who also had a chronic condition (Table A1 in S1 Text). Mental health or behavioural disorders (that were not already in the definition for "adversity") affected 33.0% to 33.5% of the girls and boys with an adversity-related injury and a chronic condition, but only 9.0% to 12.3% of the girls and boys with an accident-related injury and a chronic condition.

In the adversity-related injury cohort, girls were admitted predominantly for drug/alcohol-related (90.1%) or self-inflicted (72.4%) injury, while boys were most often admitted for violent (46.7%) or drug/alcohol-related (56.5%) injury. The distribution of ethnicity did not differ substantially between the two cohorts. The median follow-up time from the index admission ranged from 6.8 to 7.7 y in both cohorts (Table A2 in S1 Text).

Risk of Death

There were 4,782 deaths within 10 y of discharge (2,415 after adversity-related injury; 2,367 after accident-related injury) (Table A2 in S1 Text). There were twice as many deaths during the 10 y after discharge as during hospitalisation for the index admission: 71.8% of all deaths between the index admission date and 10 y later occurred after discharge from the index admission. The average time to death post-discharge in the two cohorts ranged from 3.1 y for boys admitted with accident-related injury to 4.1 y for girls admitted with accident-related injury.

At 10 y, the cumulative risk of death after hospital discharge in the adversity-related injury cohort was 7.3/1,000 for girls (equivalent to one in 137; 95% CI, one in 147 to one in 128) and 15.6/1,000 for boys (one in 64; 95% CI, one in 68 to one in 61), compared with 3.7/1,000 girls (one in 270; 95% CI, one in 294 to one in 244) and 6.0/1,000 boys (one in 167; 95% CI, one in 175 to one in 159) in the accident-related injury cohort (Table A3 in S1 Text). Risks of death after discharge were higher following adversity-related injury than accident-related injury at all time points (Figs 2 and 3), and risks after either adversity-related or accident-related injury were higher than in the general population (Fig 4). Among girls and boys, the age group with the highest risk of death was 18–19 y olds (Figs 2 and 3). For girls in this age group, one in 90 died by 10 y after discharge from an admission for an adversity-related injury compared with one in 175 after an accident-related injury (Table A3 in S1 Text). The corresponding figures for boys in this age group were one in 52 and one in 115.

On average over the 10 y after discharge, risks of death in the adversity-related injury cohort compared with the accident-related injury cohort were 61% (95% CI 43%–82%) higher in girls and 113% (95% CI 98%–129%) higher in boys, after adjusting for age (95% CIs greater than unity; Table 2). Risks of death were increased in girls and boys after all combinations of violent,

Table 1. Characteristics at discharge from index emergency admission for injury.

Characteristic	Girls		Boys	
	Adversity-Related Injury	Accident-Related Injury	Adversity-Related Injury	Accident-Related Injury
All	181,926 (100%)	166,462 (100%)	151,083 (100%)	483,356 (100%)
Age				
10–14 y old	47,926 (26.3%)	103,215 (62.0%)	24,301 (16.1%)	259,862 (53.8%)
15–17 y old	84,605 (46.5%)	36,624 (22.0%)	57,706 (38.2%)	137,044 (28.4%)
18–19 y old	49,395 (27.2%)	26,623 (16.0%)	69,076 (45.7%)	86,450 (17.9%)
History of a chronic condition	27,922 (15.3%)	18,934 (11.4%)	21,161 (14.0%)	49,436 (10.3%)
Ethnicity*				
White	144,522 (79.4%)	129,248 (77.6%)	109,307 (72.3%)	352,614 (73.0%)
Black	4,284 (2.4%)	3,320 (2.0%)	4,486 (3.0%)	9,917 (2.1%)
Asian	6,432 (3.5%)	4,066 (2.4%)	4,563 (3.0%)	13,633 (2.8%)
Mixed	2,448 (1.3%)	1,470 (0.9%)	1,540 (1.0%)	4,171 (0.9%)
Other	3,309 (1.8%)	2,541 (1.5%)	3,000 (2.0%)	7,491 (1.5%)
Missing	20,931 (11.5%)	25,817 (15.5%)	28,187 (18.7%)	95,530 (19.8%)
Deprivation based on IMD score*				
Least deprived	22,309 (12.3%)	29,002 (17.4%)	16,991 (11.2%)	85,304 (17.6%)
Second least deprived	24,941 (13.7%)	29,872 (17.9%)	19,474 (12.9%)	85,052 (17.6%)
Middle	30,698 (16.9%)	30,472 (18.3%)	24,450 (16.2%)	87,512 (18.1%)
Second most deprived	40,721 (22.4%)	32,670 (19.6%)	33,461 (22.1%)	95,821 (19.8%)
Most deprived	61,161 (33.6%)	41,923 (25.2%)	53,437 (35.4%)	122,749 (25.4%)
Missing	2,096 (1.2%)	2,523 (1.5%)	3,270 (2.2%)	6,918 (1.4%)
Type of adversity-related injury				
Any violent	13,262 (7.3%)		70,594 (46.7%)	
Any drug/alcohol-related	163,888 (90.1%)		85,421 (56.5%)	
Any self-inflicted	131,739 (72.4%)		44,621 (29.5%)	
Emergency admissions prior to index (at 10–19 y old)				
Adversity-related injury	18,311 (10.1%)	1,566 (0.9%)	8,121 (5.4%)	3,262 (0.7%)
Accident-related injury (no adversity)	5,438 (3.0%)	6,264 (3.8%)	10,328 (6.8%)	36,320 (7.5%)

Data are given as *n* (percent).

*Missing values were replaced with the modal value of admission records for that individual at 10–19 y old. If the value was still missing, it was replaced with the modal value of records for that individual at 0–30 y old.

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drug/alcohol-related, and self-inflicted injury, compared with accident-related injury (age-adjusted HRs 1.09 to 5.35; Figs 5 and S1). These risks were highest after combinations of adversity-related injury that included drug/alcohol-related injury (age-adjusted HRs: 1.61 to 5.35), though not statistically significantly for girls admitted for all three types of adversity-related injury (age-adjusted HR 2.43, 95% CI 0.91–6.51). Results of models adjusted for clinically relevant variables selected a priori are presented in Table A4 in S1 Text.

Risk of Emergency Re-admission

There were 621,050 emergency re-admissions in both cohorts in total (Table A2 in S1 Text). On average, adolescent girls and boys in the adversity-related injury cohort had their first emergency re-admission 586 and 750 d, respectively, after discharge from the index admission, 6 and 12 mo sooner than for the accident-related injury cohort.

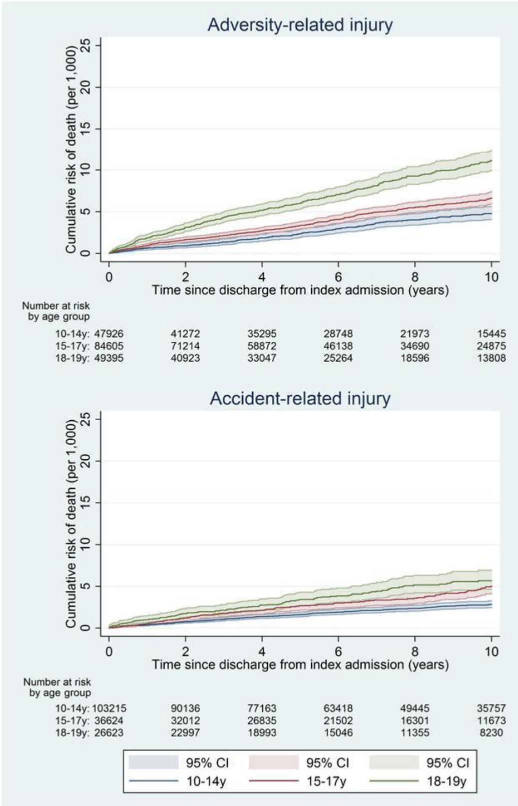

Fig 2. Cumulative risk of death in girls, by age group.

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The 10-y risk of emergency re-admission was 54.2% for girls (95% CI 53.9%–54.5%) and 40.5% for boys (95% CI 40.2%–40.9%) (Table A5 in S1 Text). The cumulative risk of emergency re-admission was higher in the adversity-related injury cohort than in the accident-related injury cohort at all time points for all age–sex groups (Figs 6 and 7). In contrast to the patterns observed for cumulative risk of death, girls had a higher risk of emergency re-admission than boys for all age groups in both cohorts at all time points. The 10-y risks of emergency re-admission were higher after all types of adversity-related injury than risks in the accident-related injury cohort, for both sexes; in boys, risks were highest after self-inflicted injury (Fig 8).

By 10 y after discharge, the risk of emergency re-admission was 76% higher for girls and 41% higher for boys in the adversity-related injury cohort than for those in the accident-related injury cohort (95% CIs for age-adjusted HRs greater than unity; Table 2). Risks of emergency re-admission were highest after an injury that included self-inflicted injury in both girls and boys (age-adjusted HRs 1.29 to 3.10; S1 Fig). Results of models adjusted for clinically relevant variables selected a priori are presented in Table A4 in S1 Text.

Risk of Multiple Emergency Re-admissions

Compared with the accident-related injury cohort, adolescents in the adversity-related injury cohort were more likely to have multiple emergency re-admissions after discharge (girls: 23.2%

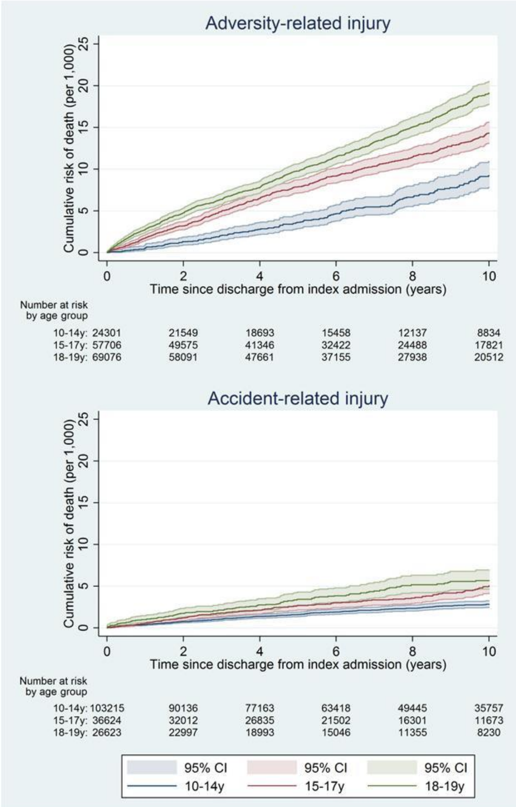

Fig 3. Cumulative risk of death in boys, by age group.

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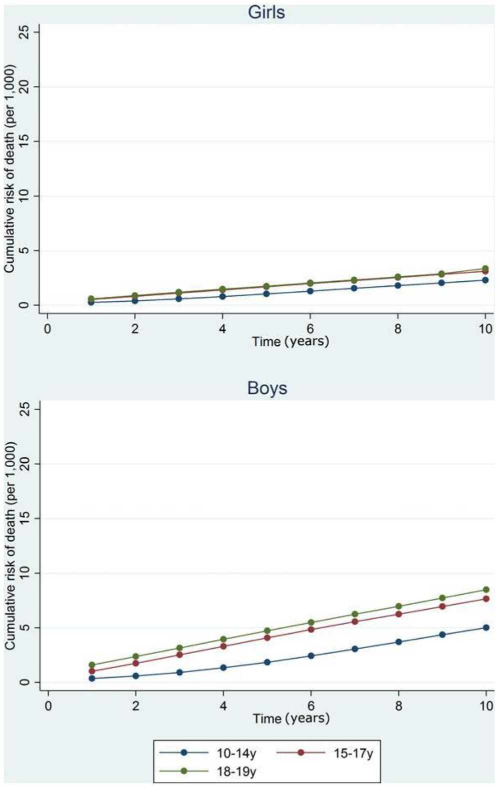

Fig 4. Estimated cumulative risk of death for girls and boys in the general population, by age group.

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versus 11.64%, boys: 13.4% versus 7·0%; Table A2 in S1 Text) and were more likely to have a higher number of re-admissions (Table A6 in S1 Text). This was the case for all combinations of adversity-related injury, after adjustment for age, in both girls and boys.

Independent Risk Factors

Relative risks of death and emergency re-admission for adversity-related injury (versus accident-related injury, estimated from Cox regression models), adjusted for age, chronic condition status, ethnicity, and deprivation are presented in Table A4 in S1 Text. In both the adversity-related and accident-related injury cohorts, presence of a chronic condition increased the risks of death and emergency admission by 2- to 5-fold in girls and boys, and girls and boys

Table 2. Relative risks of death and emergency re-admission within 10 y of index admission.

Sex and Variable at Index	HR* (95% CI)	
	Death	Emergency Re-admission
Girls		
Adversity-related (versus accident-related) injury	1.61 (1.43–1.82)	1.76 (1.74–1.79)
Age group 15–17 y (versus 10–14 y)	1.46 (1.27–1.69)	1.22 (1.20–1.23)
Age group 18–19 y (versus 10–14 y)	2.32 (2.01–2.68)	1.29 (1.27–1.31)
Boys		
Adversity-related (versus accident-related) injury	2.13 (1.98–2.29)	1.41 (1.39–1.43)
Age group 15–17 y (versus 10–14 y)	1.68 (1.54–1.84)	1.14 (1.13–1.15)
Age group 18–19 y (versus 10–14 y)	2.16 (1.98–2.37)	1.26 (1.24–1.27)

*HRs estimated from Cox regression models, where independent variables (adversity-related/accident-related injury and age group) were entered simultaneously.

doi:10.1371/journal.pmed.1001931.t002

living in the most deprived areas based on IMD score had the highest risks of death and emergency re-admissions. This association persisted across all deprivation levels for deaths in boys and for emergency admissions in girls and boys (Table A7 in S1 Text).

We found no association between ethnicity and long-term risks of death or emergency re-admission after adjusting for deprivation and underlying chronic condition (Table A4 in S1 Text). Missing information on ethnicity or deprivation was associated with reduced risks of death and emergency re-admissions in girls and boys, possibly because of a failure to link recurrent admissions for individuals with incomplete data.

Discussion

We report cumulative risks of death and emergency re-admission in adolescents in the 10 y after discharge from an admission for adversity-related injury versus accident-related injury. We found increased long-term risks of death and re-admission among adolescents discharged after hospitalisation for violent, drug/alcohol-related, or self-inflicted injury, compared with those discharged after accident-related injury. Risks of harm after both adversity-related and accident-related injury were higher than for adolescents in the general population. In the 10 y after discharge following an adversity-related injury, one in 137 girls and one in 64 boys died across all adolescent age groups. These risks for 18–19 y olds were one in 52 and one in 90. However, risks of death and re-admission were highest after any drug/alcohol-related injury or self-inflicted injury for both sexes. Having a chronic condition (typically respiratory or mental health/behavioural disorders for adolescents in this study) and living in the most deprived areas (based on residential postcode) increased the risks of death and re-admission.

Strengths and Limitations

One strength of our study is the use of administrative data to study the entire population of adolescents hospitalised with injury within the English publicly provided NHS. Second, linkage of all hospital admissions and death records made it possible to study outcomes 10 y after discharge from the index admission. Third, this is the first study to our knowledge that has quantified risks of harm in adolescents after all three of violent, drug/alcohol-related, and self-inflicted injury within the same cohort. Long-term follow-up has previously been reported only after self-inflicted injury [14].

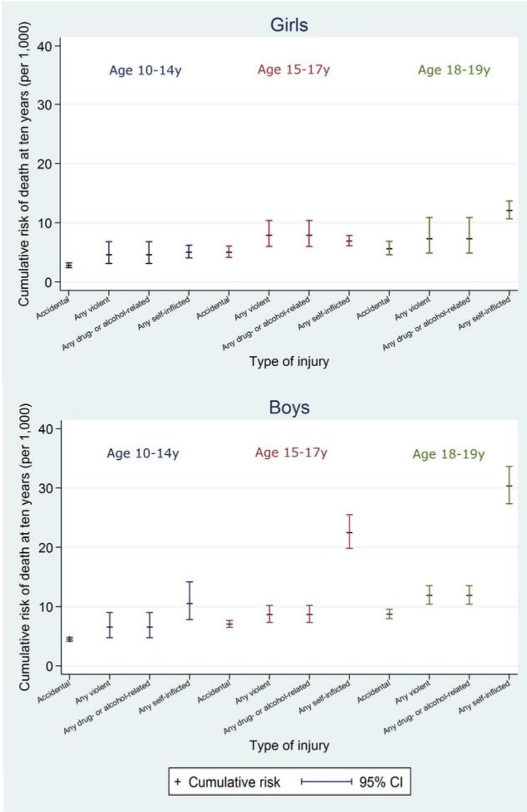

Fig 5. 10-y risk of death by type of injury.

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One limitation of our study is potential misclassification of violent, drug/alcohol-related, or self-inflicted injury as accident-related injury [32,33], which would likely lead to underestimation of the increased risk associated with adversity-related injury. For example, a study in one US hospital site showed that for up to 25% of cases of violent injury in children where violence was recorded in the medical notes, violence was not coded in the electronic discharge records [34]. Misclassification as accident-related injury may be more likely in boys, for whom behaviours such as violence or misuse of alcohol may be normalised and less likely to be noted in hospital records than for girls [35].

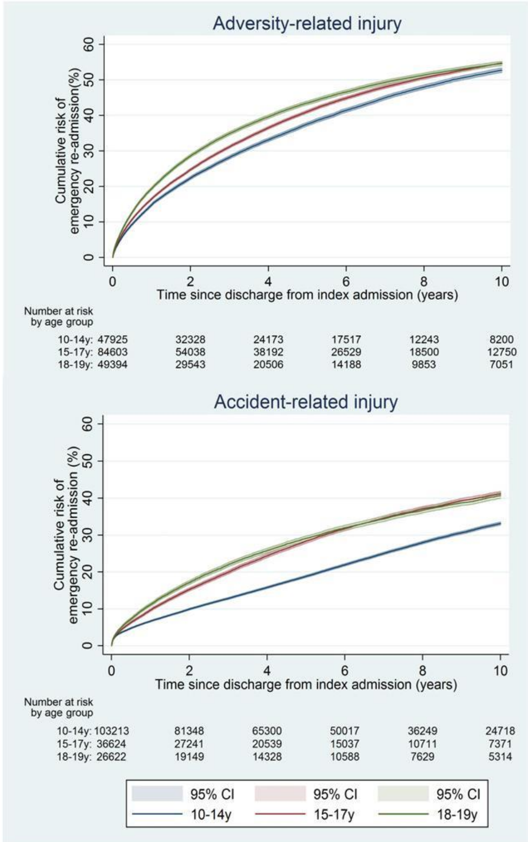

Fig 6. Cumulative risk of emergency re-admission in girls, by age group.

doi:10.1371/journal.pmed.1001931.g006

Another limitation is that linkage error may lead to a failure to capture death or re-admission and is more common in certain ethnic minorities. For example, in a study where the HES linkage algorithm was applied in another routine paediatric dataset, children and adolescents with black or "other" (i.e., not white, black, Asian, or mixed) ethnicity were approximately 2.4 to 4.1 times more likely to have a false or missed match than their white counterparts [36]. Failure to link events would favour underestimation of the risks of death and re-admission for these groups.

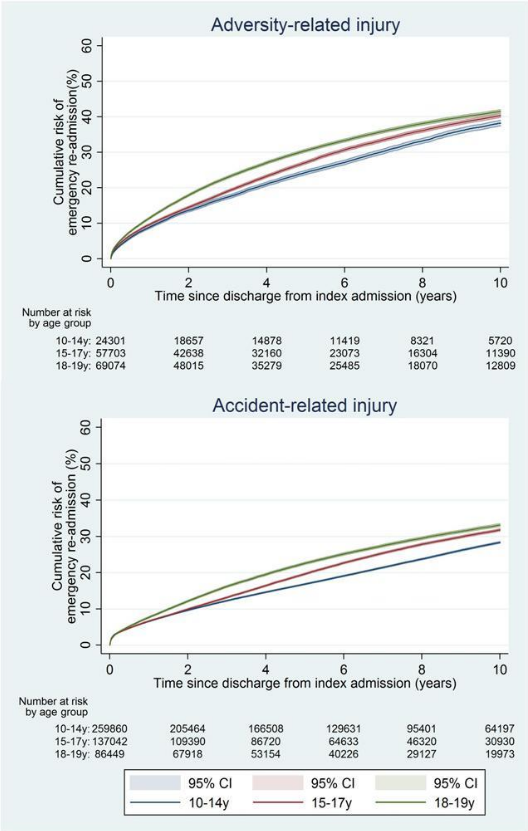

Fig 7. Cumulative risk of emergency re-admission in boys, by age group.

doi:10.1371/journal.pmed.1001931.g007

Finally, HES data do not include information on interventions received by the adolescents during or after admissions, such as referral to mental health services. Effective interventions could have confounded the association between adversity-related injury and later harm. This confounding could have caused underestimation of the association between adversity-related injury and later harm if adolescents in the adversity group were more likely to receive effective interventions than those in the accident-related injury group. In practice, however, psychosocial assessments are routinely recommended only for adolescents with self-inflicted injury [11], and it is estimated that only 60% actually receive such an assessment [37].

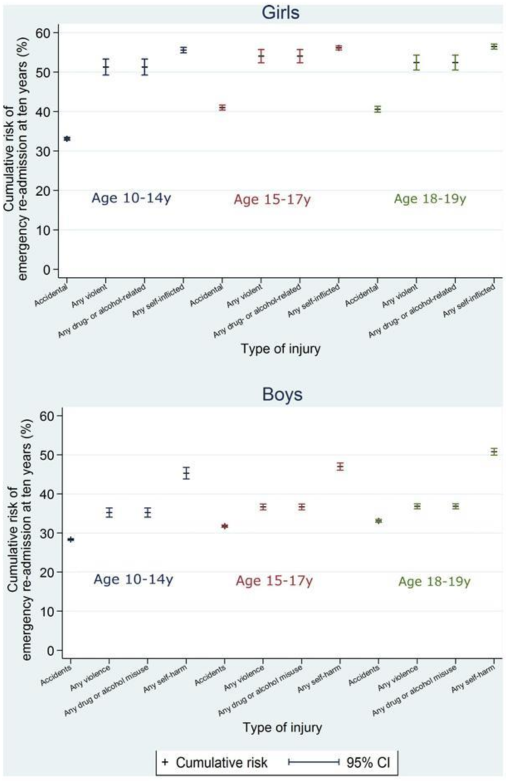

Fig 8. 10-y risk of emergency re-admission by type of injury.

doi:10.1371/journal.pmed.1001931.g008

Generalisability of the Study and Comparison with Other Findings

Our estimates of the relative increase in risks of death and emergency re-admission are likely to be generalisable to other hospitalised adolescent populations within the UK. However, generalisability to other countries and healthcare systems depends on the similarities of their populations of adolescents admitted with adversity-related injury to that of England. Generalisability also depends on the availability and intensity of psychosocial support for vulnerable adolescents after hospital discharge. Patterns of self-harm and drug/alcohol use during adolescence in other parts of Europe [4,38], but not in the US [39,40], have been shown to be similar to those in England.

Mortality rates in this study were either similar to or slightly higher than those reported for 14–24 y olds presenting with violent injury to the emergency department in the US [15]. The risk of violent death 2 y after a violent or drug/alcohol-related injury presentation (including non-admission) was 0.8/1,000. This figure is consistent with the risk of all causes of death 1 y after violent injury in our study (girls: 0.5/1,000; boys: 1.2/1,000). A prospective cohort study in England reported a mortality rate of 10/1,000 in 10–18 y olds followed for a median time period of 6 y after presentation to hospital for self-harm [14]. Our risks of mortality at 5 y after self-inflicted injury were similar (girls: 4.0/1,000; boys: 12.7/1,000).

Implications for Policy, Practice, and Research

Adolescents discharged from hospital after an adversity-related injury have substantially increased risks of death and emergency re-admission during the next 10 y compared with adolescents discharged after an accident-related injury; 10 y after discharge from hospital in England for an adversity-related injury, one in 52 boys and one in 90 girls aged 18–19 y will have died. These risks may be underestimated because of under-recording of adversity in hospital discharge records.

The risk of future harm was increased after all types of adversity-related injury. These findings justify extending national policy for psychosocial assessment after self-inflicted injury to all types of adversity-related injury. Consideration of psychological and social circumstances is good clinical practice, particularly for vulnerable adolescents. However, extending mandated psychosocial assessment from self-inflicted injury to all three types of adversity-related injury may have implications for services, as injured young people aged 16 y or older are often managed on adult surgical wards in the NHS, where expertise in psychosocial assessment and support for young people may be limited. Those who are male, older, have an underlying chronic condition, or are from deprived areas, and those exposed to multiple types adversity (e.g., drug/alcohol misuse and self-harm) have the highest risks of future harm (Table A7 in S1 Text; S1 Fig). Whether interventions should be targeted at these groups requires evidence of the effectiveness, feasibility, and cost-effectiveness of interventions.

There is a lack of evidence regarding effective interventions to reduce the risk of future harm in adolescents exposed to adversity-related injury. Our confirmation that there are increased long-term risks for these adolescents highlights the need to develop and evaluate interventions. Although some interventions in the UK for self-inflicted injury have shown positive effects, these were in samples too small to provide conclusive results [3]. Brief psychosocial interventions to address violent behaviour or alcohol misuse [41–47] have shown promise for improving outcomes and for cost-effectiveness [41,48,49], but follow-up was limited to 18 mo. In addition, these interventions have been evaluated predominantly in the US, where there are cultural differences in violence and drinking behaviours, healthcare systems, and social welfare support.

Supporting Information

S1 STROBE checklist. Items that should be included in reports of observational studies.
(DOC)

S1 Fig. Relative risks of death and emergency re-admission within 10 y of index admission, by combinations of types of adversity-related injury.
(TIF)

S1 Table. Original study's design and analysis plan and deviations from this plan for final study report.
(DOCX)

S2 Table. Derivation of 1- to 10-y risks of death in the general adolescent population.
(DOC)

S1 Text. Additional tables.
(DOC)

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Author Contributions

Conceived and designed the experiments: AH RG AG-I LL. Analyzed the data: AH. Wrote the first draft of the manuscript: AH. Contributed to the writing of the manuscript: AH RG AG-I LL AP. Agree with the manuscript's results and conclusions: AH RG AG-I LL AP. Obtained permissions to use the data: AH RG AG-I. All authors have read, and confirm that they meet, ICMJE criteria for authorship.

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Editors' Summary

Background

Adolescence—the period of human growth and development that occurs between the ages of 10 and 19 years—prepares the body and mind for adulthood. It is characterized by numerous, sometimes troubling, physical, mental, emotional, and social changes. Perhaps the biggest change is puberty, which usually occurs between the ages of 10 and 14 years for girls and between the ages of 12 and 16 years for boys. During puberty, several biological changes prepare the body for parenthood. For example, the breasts develop and menstrual periods begin in girls, and the testicles and penis grow in boys. Physiological growth is also rapid during puberty, and, by the end of puberty, both boys and girls are at or close to their adult height and weight. Adolescence is also the time when individuals begin to move towards social and economic independence, and when they acquire their own unique personality and opinions, the emotional skills needed to form adult relationships, and the intellectual capacity for abstract reasoning.

Why Was This Study Done?

Adolescents often use alcohol and other drugs unwisely, and because adolescents do not fully understand the relationships between behavior and consequences, everyday situations sometimes escalate into violence. Moreover, some adolescents intentionally damage their body (self-harm) as a way to deal with the emotional upheaval of adolescence. Consequently, adolescents often sustain adversity-related injuries (violence-related, drug- or alcohol-related, or self-inflicted injuries). In England, for example, a third of all adolescents admitted to hospital for any injury have an adversity-related injury; the remaining injuries are mainly accident-related. Because adolescents who present with an adversity-related injury often re-present later with other adversity-related injuries, hospitalization for such injuries is a "teachable moment," a time when relevant interventions (for example, psychosocial interventions that deal with psychological and social development) can potentially reduce the risk of further harm. But which adolescents are likely to benefit from such interventions depends on their long-term risks of harm. Here, the researchers use hospitalization data for England to compare the ten-year risks of mortality (death) and re-admission among adolescents after adversity-related injury with the risks after accident-related injury.

What Did the Researchers Do and Find?

The researchers used National Health Service hospital admissions data collected between 1997 and 2012 for 10–19 year olds with emergency admissions for adversity-related or accident-related injury (333,009 and 649,818 adolescents, respectively) to estimate the ten-year risks of death and emergency re-admission among injured adolescents after discharge. Among adolescents discharged after an adversity-related injury, one in 137 girls and one in 64 boys died within ten years. Also, 54.2% of girls and 40.5% of boys had a subsequent emergency re-admission for an adversity-related injury, and emergency re-admission rates were highest in 18–19 year olds. The risks of both death and emergency re-admission were higher among adolescents discharged after an adversity-related injury than among adolescents discharged after an accident-related injury. For example, boys discharged after an adversity-related injury were about twice as likely to die within the next ten years as boys discharged after an accident-related injury. Risks of death were increased after all combinations of adversity-related injury but particularly after combinations that included drug- or alcohol-related or self-inflicted injury. Finally, the risks of emergency re-admission were highest after injuries that included self-inflicted injury in both girls and boys.

What Do These Findings Mean?

These findings indicate that adolescents discharged from the hospital after an admission for violence-related, drug- or alcohol-related, or self-inflicted injuries have increased risks of subsequent harm up to a decade later. Misclassification of some adversity-related injuries as accident-related injuries may affect the accuracy of these findings. Another important limitation of this observational study is residual confounding. That is, although the researchers adjusted for known factors likely to affect the risk of re-admission or death in their analysis, the adolescents who were re-admitted or died subsequent to discharge after an adversity-related injury may have shared other unknown characteristics that were responsible for their increased risk of harm. Nevertheless, these findings identify several risk factors that clinicians and service providers can use to identify those adolescents admitted to hospital with an injury who are at high or low risk of subsequent harm. Specifically, these findings suggest that the introduction of strategies for reducing subsequent harm after discharge should be considered for all types of adversity-related injury, particularly when it occurs in older adolescents.

Additional Information

This list of resources contains links that can be accessed when viewing the PDF on a device or via the online version of the article at http://dx.doi.org/10.1371/journal.pmed.1001931.

- The World Health Organization (WHO) provides brief information on adolescence (in several languages) and links to WHO documents concerned with adolescent health
- The UK Royal College of Psychiatrists provides a fact sheet on surviving adolescence for parents, teachers, and young people
- The American Academy of Pediatrics also provides information on the stages of adolescence (in English and Spanish)
- The UK not-for-profit organization Young Minds has real stories about self-harm and about other aspects of emotional well-being and mental health among young people
- MedlinePlus provides basic information and links to further resources about adolescent development, self-harm, teen violence, and injuries
- A previous open-access paper by the researchers about violence, self-harm, and drug or alcohol misuse among adolescents admitted to the hospital for injuries is available

E. Supplementary tables: Study I

E.1 Numbers of adolescents admitted with multiple types of adversity-related injury at 10-19 years old, who had all types recorded at the same admission

Adolescent group	Number of adolescents	All types of adversity-related injury recorded at same emergency admission, N (%)
Girls		
V + SI	130	84 (64.6)
V + DA	862	679 (78.8)
SI + DA	50,404	50,239 (99.7)
V + SI + DA	1,485	503 (33.9)
Boys		
V + SI	217	87 (40.1)
V + DA	6,013	5,055 (84.1)
SI + DA	16,953	16,794 (99.1)
V + SI + DA	1,657	332 (20.0)

V = Violent injury; SI = Self-inflicted injury; DA = Drug/alcohol-related injury

E.2 Numbers of emergency admissions for adversity-related injury, by adolescent groups and types of adversity-related injury*

	Number of emergency admissions for injury (% of Total)									
Adolescent group	**Total**	**V only**	**SI only**	**DA only**	**V + SI**	**V + DA**	**SI + DA**	**V + SI + DA**	**Accidents**	**Other**
Girls										
V only	5,878 (100.0)	4,327 (73.6)							380 (6.5)	1,171 (19.9)
SI only	4,652 (100.0)		2,658 (57.1)						531 (11.4)	1,463 (31.4)
DA only	22,475 (100.0)			15,711 (69.9)					1,575 (7.0)	5,189 (23.1)
V + SI	369 (100.0)	87 (23.6)	99 (26.8)		100 (27.1)				17 (4.6)	66 (17.9)
V + DA	1,771 (100.0)	346 (19.5)		308 (17.4)		734 (41.4)			87 (4.9)	296 (16.7)
SI + DA	109,051 (100.0)		7,548 (6.9)	5,259 (4.8)			71,808 (65.8)		4,128 (3.8)	20,308 (18.6)
V + SI + DA	8,268 (100.0)	1,114 (13.5)	519 (6.3)	810 (9.8)	306 (3.7)	242 (2.9)	3,246 (39.3)	631 (7.6)	290 (3.5)	1,110 (13.4)
Accidents Only									64,592 (73.2)	23,591 (26.8)
Boys										
V only	39,721 (100.0)	29,766 (74.9)							5,546 (14.0)	4,409 (11.1)
SI only	5,312 (100.0)		2,615 (49.2)						1,205 (22.7)	1,492 (28.1)
DA only	29,276 (100.0)			18,765 (64.1)					5,540 (18.9)	4,971 (17.0)
V + SI	719 (100.0)	254 (35.3)	1,641 (13.1)		5,540 (44.1)				93 (12.9)	100 (13.9)
V + DA	12,552 (100.0)	2,421 (19.3)		165 (22.9)		107 (14.9)			1,675 (13.3)	1,275 (10.2)
SI + DA	36,646 (100.0)		3,667 (10.0)	1,654 (4.5)			22,677 (61.9)		3,813 (10.4)	4,835 (13.2)
V + SI + DA	7,149 (100.0)	1,536 (21.5)	637 (8.9)	337 (4.7)	538 (7.5)	106 (1.5)	2,258 (31.6)	394 (5.5)	593 (8.3)	750 (10.5)
Accidents Only									200,233 (80.1)	49,853 (19.9)

V = Violent injury, SI = Self-inflicted injury, DA = Drug/alcohol-related injury
*according to types of adversity-related injury and accident-related injury between 10 and 19 years old (inclusive)

F. Example to illustrate statistical methods discussed in Chapter 5

To demonstrate the methods described in Chapter 5 I use the example of quantifying the risk of an event in adolescent girls in the HES database. Specifically, I define the index admission as the first emergency admission for injury at 10-19 years old and the event as death after discharge from this index admission (Figure). At times, I also report the risk of death in this example.

There were 388,937 girls with an emergency admission for injury in my extract of HES-ONS, of which 44% had adversity-related injury (n=180,576) and 46% had accident related injury (n=168,244) at their index admission. The remaining 39,117 girls with neither adversity- nor accident-related injury at their index admission are not discussed any further for the purposes of this example. Girls in the adversity-related and accident-related injury groups were followed up for around seven to eight years, with a maximum possible follow-up of 15 years. Among girls in the adversity-related injury group, 1,077 (0.57%) died within the ten years after discharge and 84,019 (49.6%) had an observed emergency re-admission, compared with 804 (0.48%) and 50,526 (28.0%) in the accident-related injury group. Further details on the two groups are provided in the Table.

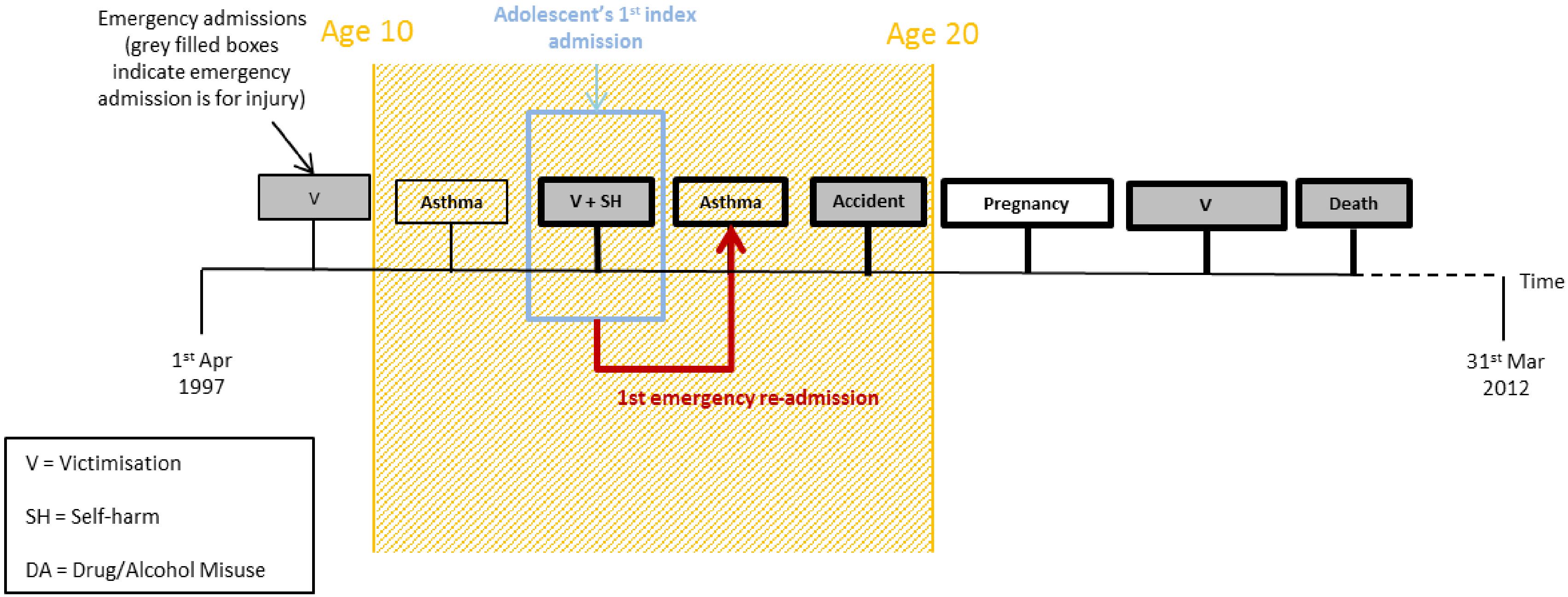


Figure: Hypothetical trajectory of an adolescent girl's admissions, illustrating how index admission and 1st event were defined

Table: Descriptive statistics of outcomes in girls discharged from an emergency admission for injury between 10 and 19y in April 1997-March 2012.

	Type of first emergency admission for injury	
Variable, units	**Adversity-related**	**Accident-related**
Number of adolescents, n	180,576	169,244
Follow-up in years, Median (IQR)	7.7 (4.0, 11.4)	7.0 (3.5, 11.0)
Died during index admission, n (per 1,000)	117 (0.65)	300 (1.8)
Died within ten years post-discharge, n (per 1,000)	1,022 (5.7)	804 (4.8)
Had an emergency re-admission within ten years post-discharge, n (per 100)	84,012 (46.5)	50,523 (29.8)
1	36,128 (20.0)	28,179 (16.6)
2	17,855 (9.9)	10,025 (5.9)
3-5	19,584 (10.8)	8,580 (5.1)
6+	10,445 (5.8)	3,739 (2.2)
Total number of emergency re-admissions		
Time to 1st emergency re-admission in days, Median (IQR)	518 (153, 1,293))	925 (246, 1,982)
Time between 1st and 2nd emergency re-admission in days, Median (IQR)	304 (77, 845)	391 (89, 1,060))
Time between 2nd and 3rd emergency re-admission in days, Median (IQR)	225 (56, 653)	247 (56, 686)

G. Supplementary tables and figures: Study II

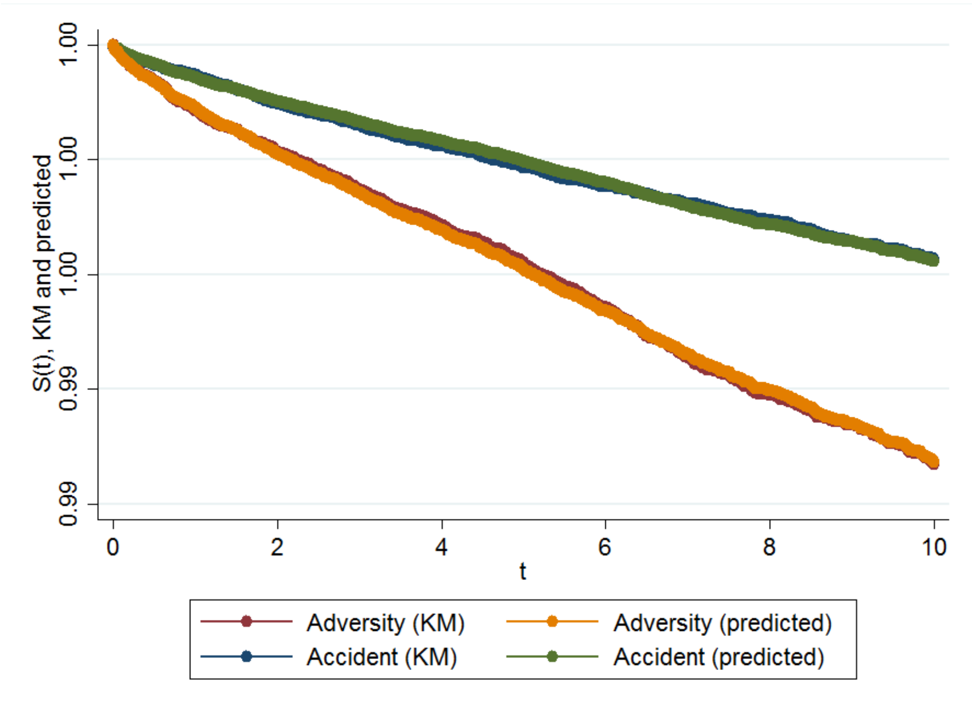
G.1 Derivation of one- to ten-year risks of death in the general adolescent population

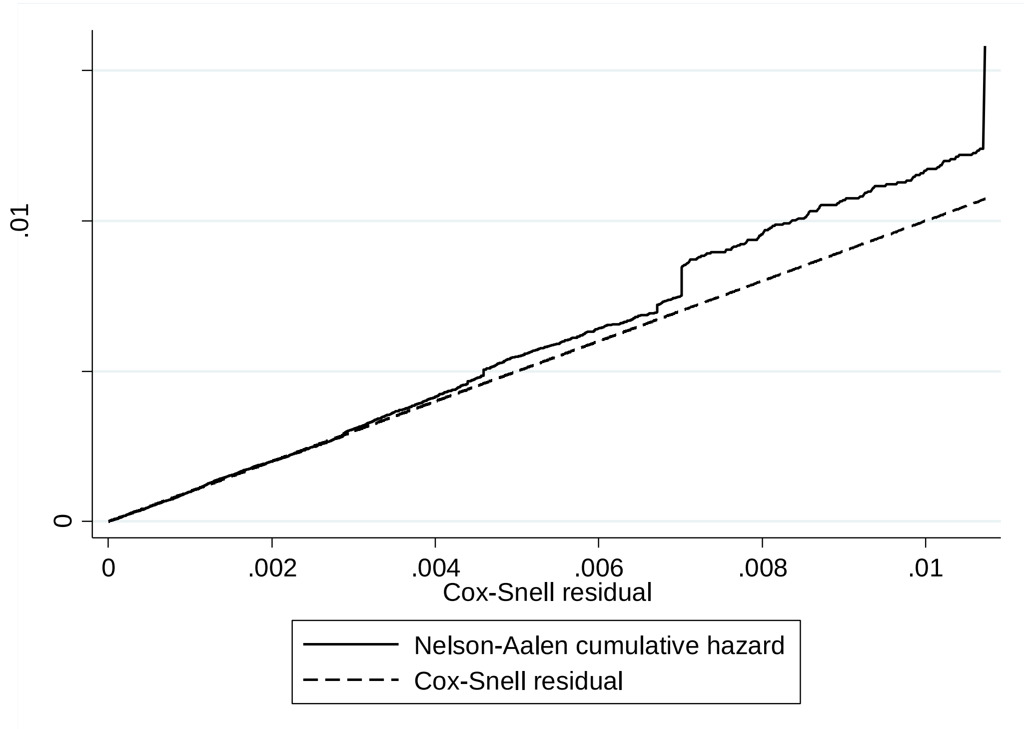
		Pr(death at given age and within given time period)										
Sex	**Age**	**1997-99**	**1998-2000**	**1999-2001**	**2000-02**	**2001-03**	**2002-04**	**2003-05**	**2004-06**	**2005-07**	**2006-08**	**2007-09**
Girls	10	0.000124	0.000110	0.000104	0.000096	0.000099	0.000105	0.000093	0.000079	0.000091	0.000084	0.000088
	11	0.000113	0.000120	0.000121	0.000102	0.000100	0.000082	0.000089	0.000086	0.000093	0.000089	0.000089
	12	0.000143	0.000132	0.000116	0.000107	0.000128	0.000135	0.000138	0.000116	0.000114	0.000098	0.000098
	13	0.000135	0.000121	0.000103	0.000105	0.000101	0.000114	0.000114	0.000124	0.000118	0.000116	0.000109
	14	0.000143	0.000141	0.000134	0.000151	0.000154	0.000153	0.000134	0.000123	0.000125	0.000108	0.000111
	15	0.000204	0.000163	0.000172	0.000148	0.000151	0.000145	0.000146	0.000153	0.000137	0.000143	0.000135
	16	0.000254	0.000247	0.000222	0.000239	0.000234	0.000226	0.000214	0.000212	0.000197	0.000169	0.000165
	17	0.000302	0.000281	0.000274	0.000256	0.000257	0.000239	0.000225	0.000229	0.000238	0.000232	0.000210
	18	0.000302	0.000322	0.000314	0.000307	0.000268	0.000260	0.000258	0.000262	0.000258	0.000257	0.000243
	19	0.000289	0.000302	0.000287	0.000306	0.000301	0.000331	0.000314	0.000293	0.000252	0.000246	0.000237
Boys	10	0.000146	0.000137	0.000141	0.000127	0.000110	0.000104	0.000109	0.000123	0.000100	0.000101	0.000089
	11	0.000160	0.000138	0.000132	0.000138	0.000144	0.000128	0.000118	0.000121	0.000128	0.000112	0.000100
	12	0.000171	0.000161	0.000172	0.000156	0.000156	0.000142	0.000158	0.000151	0.000140	0.000115	0.000106
	13	0.000188	0.000174	0.000175	0.000195	0.000198	0.000180	0.000163	0.000167	0.000171	0.000154	0.000139
	14	0.000249	0.000223	0.000220	0.000218	0.000223	0.000210	0.000201	0.000193	0.000187	0.000170	0.000157
	15	0.000275	0.000246	0.000240	0.000258	0.000260	0.000271	0.000248	0.000236	0.000232	0.000228	0.000246
	16	0.000448	0.000424	0.000374	0.000381	0.000363	0.000358	0.000331	0.000333	0.000332	0.000337	0.000308
	17	0.000594	0.000561	0.000567	0.000550	0.000538	0.000524	0.000520	0.000532	0.000520	0.000495	0.000468
	18	0.000791	0.000782	0.000781	0.000784	0.000756	0.000695	0.000662	0.000623	0.000588	0.000555	0.000533
	19	0.000844	0.000818	0.000818	0.000781	0.000738	0.000656	0.000647	0.000651	0.000641	0.000615	0.000586

I derived the above table using the freely-available Excel document 'England, National Life-tables, 1980-1982 to 2011-2013 (Excel sheet, 920kB)': http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-365199. I derived estimates for 1, 2,… 10 –year risks of death for a cohort of 10-19 year olds in 1997-1999 (thus 10-year estimates were available for the entire cohort). For example, the 1-year risk of death for a 10 year old in 1997-1999 was estimated as Pr(death at 10 years old in 1997-1999 or at 11 years old in 1998-2000) = 0.000124 + 0.000120.

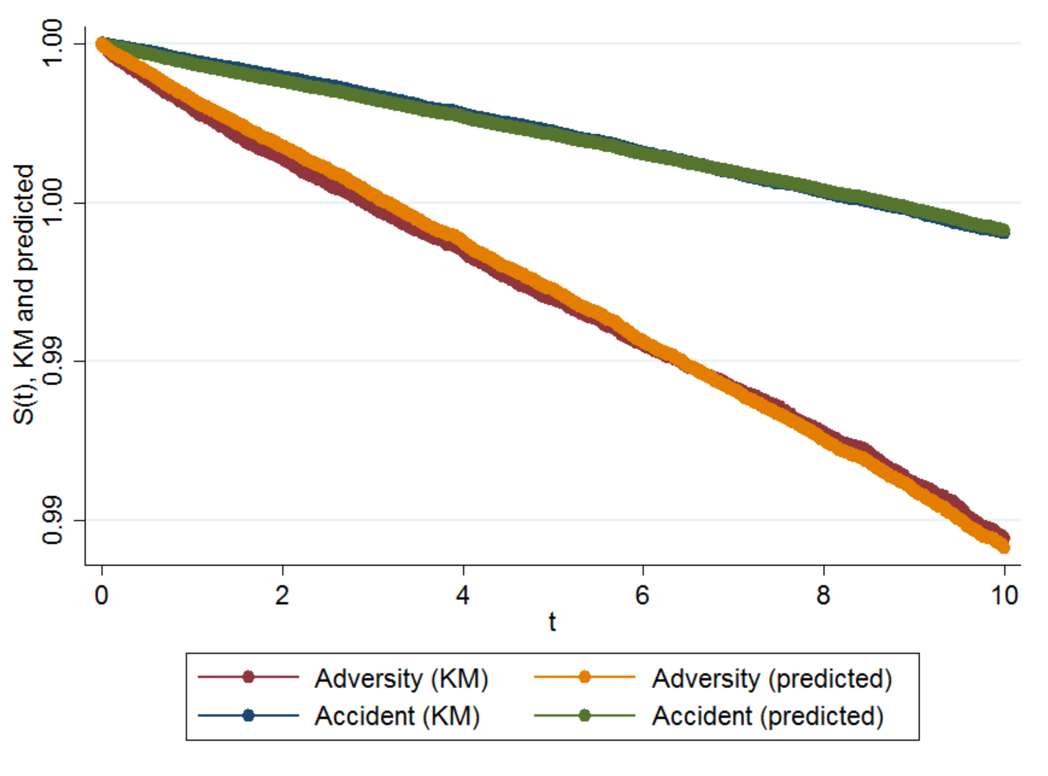
G.2 Graphical tests for proportionality of hazards and goodness-of-fit of semi-parametric proportional hazards models

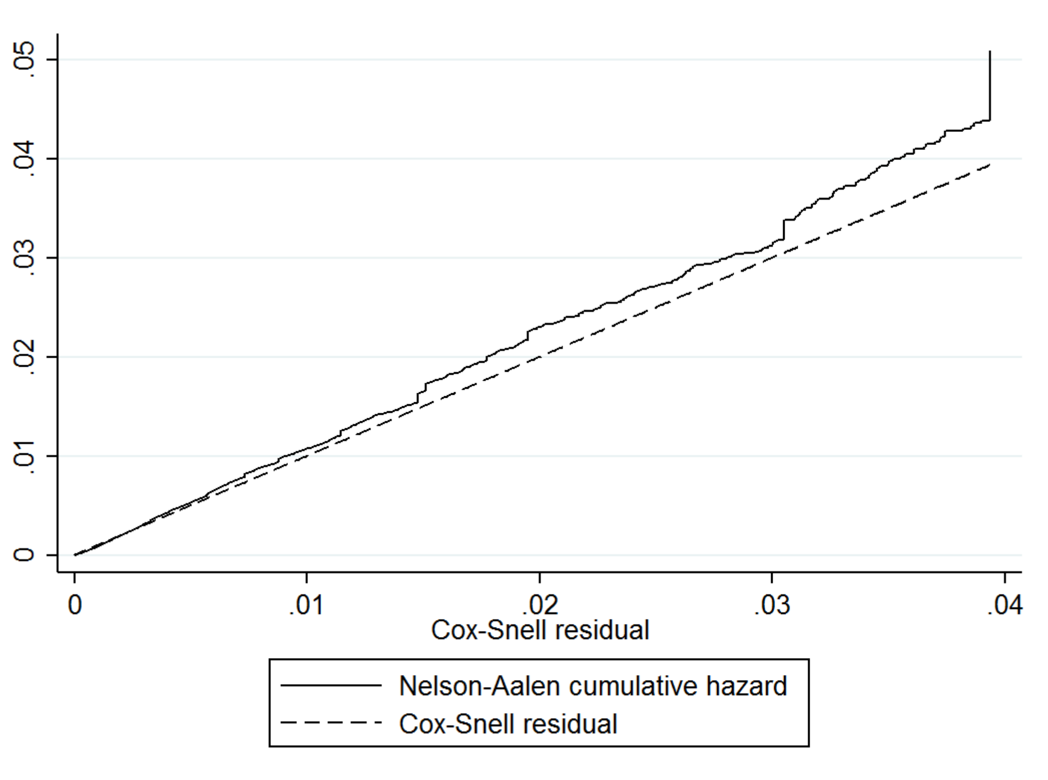
a) Girls: event is death and adversity (vs. accident) -related injury and age-group (18-19y and 15-17y vs. 10-14y) are covariates



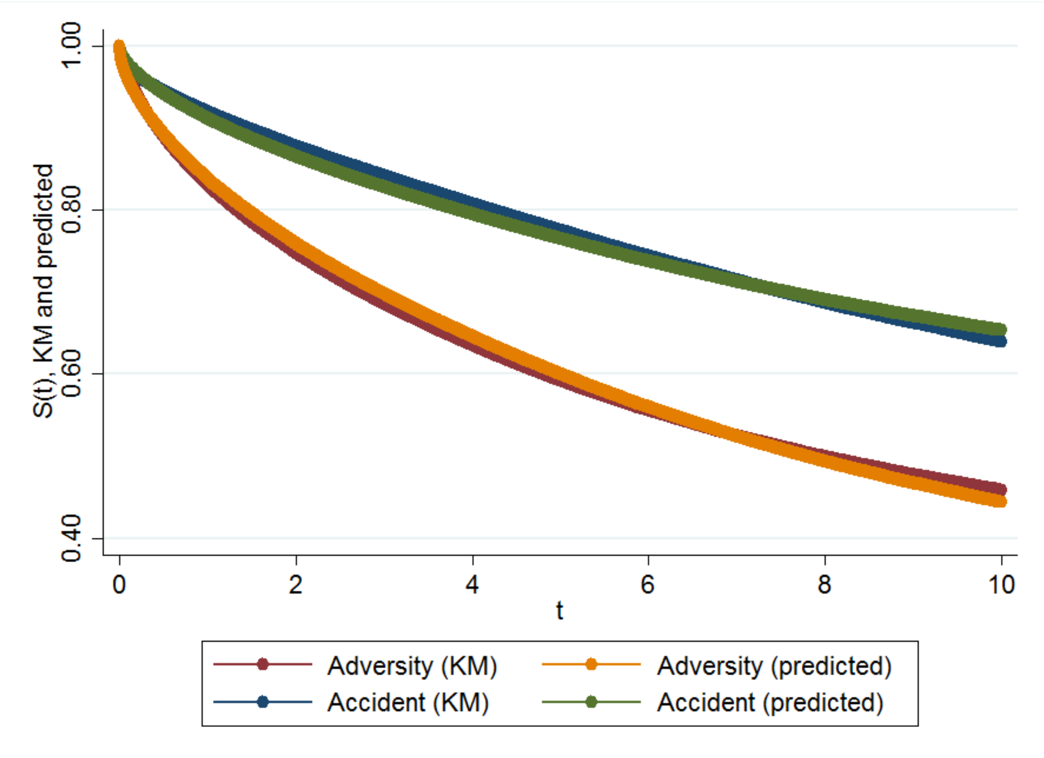


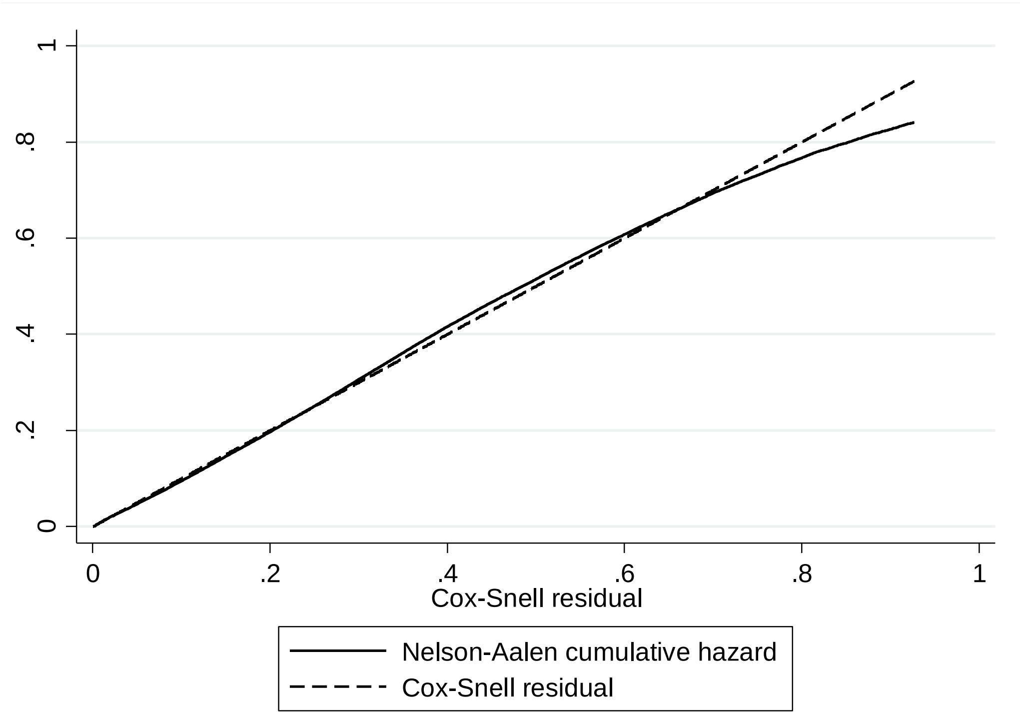
b) Boys: event is death and adversity (vs. accident) -related injury and age-group (18-19y and 15-17y vs. 10-14y) are covariates



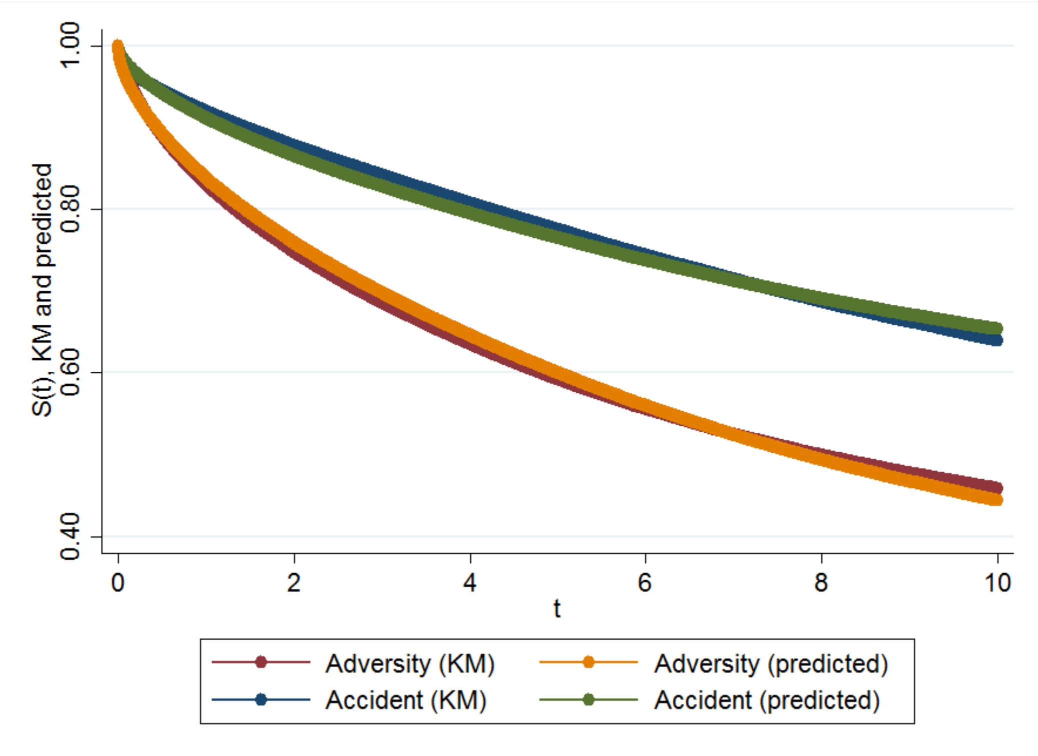


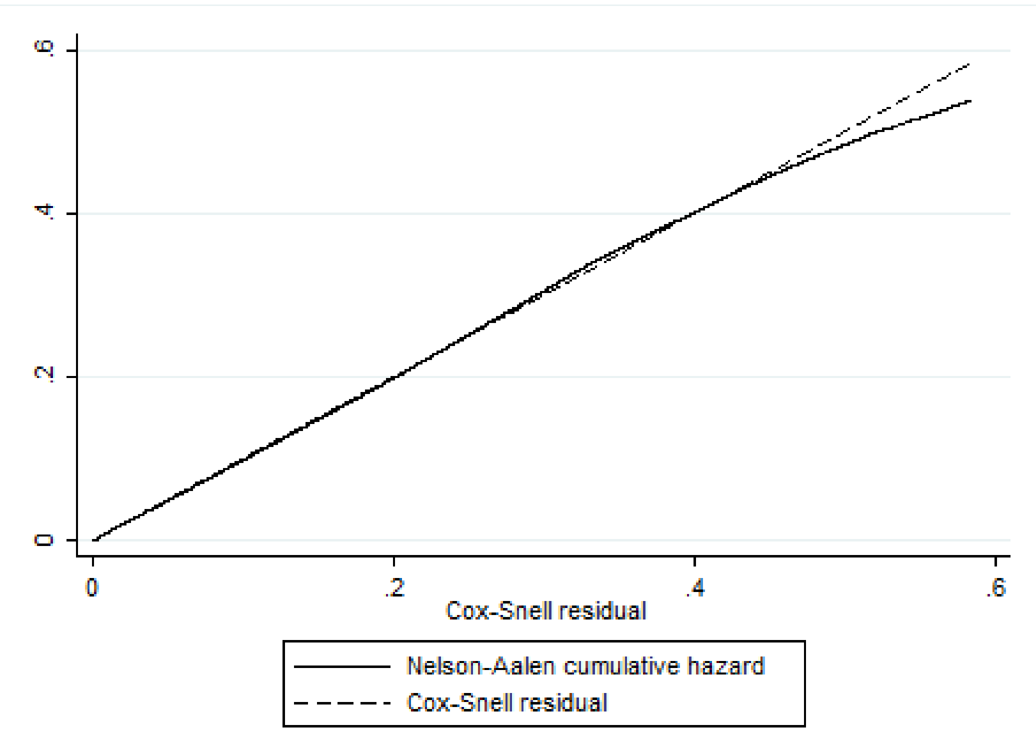
a) *Girls: event is emergency re-admission and adversity (vs. accident) - related injury and age-group (18-19y and 15-17y vs. 10-14y) are covariates*





d) *Boys: event is emergency re-admission and adversity (vs. accident) - related injury and age-group (18-19y and 15-17y vs. 10-14y) are covariates*





G.3 p-values from formal statistical tests for proportionality of hazards and goodness-of-fit of semi-parametric proportional hazards models

	Statistical test (null hypothesis)		
Sex / **Outcome**	**Schoenfeld residuals (slope = 0)**	**Interaction between adversity-related injury and time (coefficient = 0)**	**Link test ([model specification]^2 = 0)**
Girls			
Death	0.234	0.336	0.378
Emergency re-admission	0.000	0.000	0.000
Boys			
Death	0.000	0.000	0.570
Emergency re-admission	0.000	0.000	0.057

p-values presented to 3 decimal places.
Model specification: independent variables for adversity-related (vs. accident related) injury, 15-17y (vs. 10-14y) and 18-19y (vs. 10-14y).

G.4 Numbers and risks of death and emergency re-admission, in ten years after discharge from index admission

Sex: Age-group Injury at index	At discharge Adolescents	1 year following discharge Followed	Died	Risk/1,000 (95% CI)	5 years following discharge Followed	Died	Risk/1,000 (95% CI)	10 years following discharge Followed	Died	Risk/1,000 (95% CI)
Girls: 10-14 years										
Adversity-related	47,926	44,604	30	0.6 (0.5, 0.9)	31,981	95	2.4 (1.9, 2.9)	15,448	155	4.8 (4.1, 5.6)
Any V*	3,931	3,650	1	0.3 (0.0, 1.9)	2,521	8	2.4 (1.2, 4.9)	1,111	12	4.3 (2.4, 7.6)
Any SI*	32,335	29,706	19	0.6 (0.4, 1.0)	20,501	53	2.0 (1.5, 2.6)	9,298	99	5.0 (4.1, 6.2)
Any DA*	41,996	39,225	28	0.7 (0.5, 1.0)	28,551	82	2.3 (1.9, 2.9)	14,026	135	4.7 (3.9, 5.6)
Accident-related	103,215	96,671	39	0.4 (0.3, 0.5)	70,480	145	1.6 (1.4, 1.9)	35,772	211	2.8 (2.5, 3.3)
Girls: 15-17 years										
Adversity-related	84,605	78,004	79	1.0 (0.8, 1.2)	52,230	235	3.4 (2.9, 3.8)	24,882	364	6.7 (6.0, 7.5)
Any V*	5,277	4,931	2	0.4 (0.1, 1.6)	3,388	11	2.7 (1.5, 4.9)	1,466	26	8.1 (5.4, 12.0)
Any SI*	63,589	58,107	63	1.0 (0.8, 1.3)	37,742	182	3.5 (3.0, 4.1)	17,456	272	6.8 (6.0, 7.7)
Any DA*	77,240	71,230	74	1.0 (0.8, 1.2)	47,888	208	3.2 (2.8, 3.7)	23,104	320	6.4 (5.7, 7.2)
Accident-related	36,624	34,470	20	0.6 (0.4, 0.9)	24,217	84	2.7 (2.2, 3.3)	11,679	122	5.0 (4.2, 6.1)
Girls: 18-19 years										
Adversity-related	49,395	45,329	89	1.9 (1.5, 2.3)	28,975	246	6.0 (5.3, 6.8)	13,813	354	11.1 (10.0, 12.4)
Any V*	4,075	3,808	3	0.7 (0.2, 2.3)	2,551	10	2.8 (1.5, 5.2)	1,191	16	6.1 (3.6, 10.5)
Any SI*	35,969	32,976	74	2.1 (1.7, 2.7)	20,668	201	6.8 (5.9, 7.8)	9,737	280	11.9 (10.5, 13.5)
Any DA*	44,822	41,003	81	1.9 (1.5, 2.3)	26,122	221	6.0 (5.2, 6.8)	12,504	321	11.2 (10.0, 12.6)
Accident-related	26,623	24,920	26	1.0 (0.7, 1.5)	17,082	77	3.4 (2.7, 4.3)	8,234	106	5.7 (4.7, 6.9)
Girls: All										
Adversity-related	181,926	167,937	198	1.1 (1.0, 1.3)	113,186	576	3.8 (3.5, 4.1)	54,143	873	7.3 (6.8, 7.8)
Any V*	13,283	12,389	6	0.5 (0.2, 1.0)	8,459	29	2.6 (1.8, 3.8)	3,767	54	6.4 (4.8, 8.4)
Any SI*	131,893	120,789	156	1.2 (1.1, 1.4)	78,911	436	4.0 (3.7, 4.4)	36,491	651	7.7 (7.1, 8.4)
Any DA*	164,058	151,458	183	1.2 (1.0, 1.3)	102,561	511	3.7 (3.4, 4.1)	49,634	776	7.2 (6.7, 7.7)
Accident-related	166,462	156,061	85	0.5 (0.4, 0.6)	111,779	306	2.1 (1.9, 2.4)	55,685	439	3.7 (3.4, 4.1)

Sex: Age-group Injury at index	At discharge	1 year following discharge			5 years following discharge			10 years following discharge		
	Adolescents	Followed	Died	Risk/1,000 (95% CI)	Followed	Died	Risk/1,000 (95% CI)	Followed	Died	Risk/1,000 (95% CI)
Boys: 10-14 years										
Adversity-related	24,301	22,923	13	0.6 (0.3, 0.9)	17,147	75	3.6 (2.9, 4.6)	8,838	146	9.2 (7.8, 10.9)
Any V*	10,561	9,946	4	0.4 (0.1, 1.1)	7,269	22	2.4 (1.6, 3.7)	3,440	42	6.6 (4.7, 9.0)
Any SI*	6,641	6,207	2	0.3 (0.1, 1.2)	4,568	21	3.9 (2.6, 6.0)	2,332	45	10.5 (7.8, 14.2)
Any DA*	12,927	12,237	8	0.6 (0.3, 1.3)	9,426	49	4.4 (3.3, 5.9)	5,182	98	11.1 (9.0, 13.6)
Accident-related	259,862	243,402	75	0.3 (0.2, 0.4)	177,108	381	1.7 (1.6, 1.9)	88,129	747	4.5 (4.2, 4.8)
Boys: 15-17 years										
Adversity-related	57,706	53,619	97	1.7 (1.4, 2.1)	37,006	380	7.9 (7.1, 8.7)	17,827	551	14.3 (13.1, 15.6)
Any V*	27,177	25,679	21	0.8 (0.5, 1.2)	17,993	107	4.7 (3.9, 5.6)	8,141	158	8.7 (7.3, 10.2)
Any SI*	17,747	16,281	55	3.2 (2.5, 4.2)	10,745	190	13.1 (11.4, 15.1)	5,407	265	22.5 (19.8, 25.5)
Any DA*	32,281	29,421	77	2.5 (2.0, 3.1)	20,120	274	10.4 (9.2, 11.7)	10,106	398	18.9 (17.0, 20.9)
Accident-related	137,044	129,506	99	0.7 (0.6, 0.9)	93,420	419	3.6 (3.3, 4.0)	43,892	660	7.1 (6.5, 7.7)
Boys: 18-19 years										
Adversity-related	69,076	63,427	186	2.8 (2.4, 3.2)	42,347	561	9.8 (9.0, 10.6)	20,519	845	19.1 (17.8, 20.5)
Any V*	32,981	30,925	56	1.7 (1.3, 2.3)	21,267	176	6.2 (5.4, 7.2)	9,689	260	11.9 (10.4, 13.5)
Any SI*	20,352	18,679	89	4.5 (3.7, 5.6)	12,114	258	15.5 (13.7, 17.5)	6,334	394	30.4 (27.4, 33.7)
Any DA*	40,326	35,981	142	3.7 (3.1, 4.3)	23,164	407	12.6 (11.5, 13.9)	11,632	616	25.1 (23.1, 27.3)
Accident-related	86,450	82,223	89	1.1 (0.9, 1.3)	59,269	338	4.5 (4.1, 5.0)	28,385	521	8.7 (8.0, 9.5)
Boys: All										
Adversity-related	151,083	139,969	296	2.0 (1.8, 2.3)	96,500	1016	8.0 (7.6, 8.6)	47,184	1542	15.6 (14.8, 16.4)
Any V*	70,719	66,550	81	1.2 (0.9, 1.5)	46,529	305	5.0 (4.5, 5.7)	21,270	460	9.8 (8.9, 10.8)
Any SI*	44,740	41,167	146	3.4 (2.9, 4.0)	27,426	469	12.7 (11.6, 14.0)	14,073	704	24.1 (22.3, 26.1)
Any DA*	85,534	77,639	227	2.8 (2.4, 3.2)	52,710	730	10.4 (9.7, 11.2)	26,920	1112	20.3 (19.1, 21.6)
Accident-related	483,356	455,131	263	0.6 (0.5, 0.6)	329,797	1138	2.8 (2.6, 2.9)	160,406	1928	6.0 (5.7, 6.3)

Sex: Age-group Injury at index	At discharge	1 year since discharge			5 years since discharge			10 years since discharge		
	Adolescents	Followed	Re-admitted	Risk/100 (95% CI)	Followed	Re-admitted	Risk/100 (95% CI)	Followed	Re-admitted	Risk/100 (95% CI)
Girls: 10-14 years										
Adversity-related	47,926	38,165	6,921	14.8 (14.5, 15.2)	20,608	15,926	37.6 (37.1, 38.1)	8,203	19,879	52.7 (52.2, 53.3)
Any V*	3,931	3,215	472	12.4 (11.4, 13.4)	1,690	1,202	35.3 (33.7, 37.0)	605	1,521	51.4 (49.4, 53.4)
Any SI*	32,335	24,865	5,254	16.8 (16.4, 17.2)	12,608	11,461	40.6 (40.0, 41.2)	4,720	13,939	55.6 (54.9, 56.3)
Any DA*	41,996	33,619	5,995	14.7 (14.3, 15.0)	18,406	13,966	37.4 (36.9, 37.9)	7,446	17,502	52.5 (51.9, 53.1)
Accident-related	103,215	90,283	6,777	6.7 (6.5, 6.8)	57,631	17,015	18.8 (18.6, 19.1)	24,730	24,911	33.1 (32.8, 33.5)
Girls: 15-17 years										
Adversity-related	84,605	65,369	13,567	16.5 (16.3, 16.8)	31,727	30,141	41.1 (40.7, 41.4)	12,754	35,902	54.7 (54.3, 55.2)
Any V*	5,277	4,224	750	14.6 (13.6, 15.6)	2,078	1,895	40.9 (39.5, 42.4)	760	2,246	54.1 (52.4, 55.8)
Any SI*	63,589	48,142	10,769	17.5 (17.2, 17.8)	22,329	23,238	42.6 (42.2, 43.1)	8,750	27,351	56.2 (55.7, 56.7)
Any DA*	77,240	59,841	12,209	16.3 (16.1, 16.6)	29,136	27,341	40.8 (40.5, 41.2)	11,866	32,662	54.6 (54.1, 55.0)
Accident-related	36,624	31,163	3,470	9.7 (9.4, 10.0)	17,648	9,079	28.3 (27.8, 28.8)	7,377	11,533	41.2 (40.5, 41.8)
Girls: 18-19 years										
Adversity-related	49,395	36,701	9,290	19.4 (19.0, 19.8)	16,989	18,741	43.5 (43.0, 44.0)	7,056	21,320	54.6 (54.0, 55.2)
Any V*	4,075	3,187	659	16.6 (15.5, 17.8)	1,562	1,474	41.0 (39.3, 42.6)	639	1,710	52.5 (50.6, 54.4)
Any SI*	35,969	26,267	7,222	20.7 (20.3, 21.2)	11,784	14,208	45.4 (44.8, 45.9)	4,820	16,075	56.6 (55.9, 57.2)
Any DA*	44,822	33,200	8,400	19.4 (19.0, 19.7)	15,292	16,958	43.6 (43.1, 44.1)	6,361	19,285	54.7 (54.1, 55.2)
Accident-related	26,623	22,182	2,901	11.2 (10.8, 11.5)	12,381	6,797	29.1 (28.5, 29.7)	5,318	8,346	40.7 (40.0, 41.5)
Girls: All										
Adversity-related	181,926	140,235	29778	16.9 (16.7, 17.0)	69,324	64,808	40.8 (40.6, 41.0)	28,013	77,101	54.2 (53.9, 54.5)
Any V*	13,283	10,626	1881	14.5 (13.9, 15.2)	5,328	4,571	39.3 (38.4, 40.2)	2,002	5,477	52.8 (51.8, 53.9)
Any SI*	131,893	99,274	23245	18.2 (18.0, 18.4)	46,721	48,907	42.9 (42.6, 43.2)	18,290	57,365	56.2 (55.8, 56.5)
Any DA*	164,058	126,660	26604	16.7 (16.5, 16.9)	62,834	58,265	40.7 (40.4, 40.9)	25,673	69,449	54.1 (53.8, 54.4)
Accident-related	166,462	143,628	13148	8.1 (7.9, 8.2)	87,660	32,891	22.5 (22.3, 22.8)	37,425	44,790	36.1 (35.8, 36.4)

	At discharge	1 year since discharge			5 years since discharge			10 years since discharge		
Sex: Age-group Injury at index	**Adolescents**	**Followed**	**Re-admitted**	**Risk/100 (95% CI)**	**Followed**	**Re-admitted**	**Risk/100 (95% CI)**	**Followed**	**Re-admitted**	**Risk/100 (95% CI)**
Boys: 10-14 years										
Adversity-related	24,301	20,897	2,129	8.9 (8.6, 9.3)	13,121	5,274	24.3 (23.7, 24.9)	5,724	7,151	38.2 (37.5, 39.0)
Any V*	10,561	9,252	729	7.1 (6.6, 7.6)	5,737	1,967	21.2 (20.4, 22.1)	2,280	2,724	35.2 (34.1, 36.4)
Any SI*	6,641	5,427	820	12.7 (11.9, 13.5)	3,243	1,829	30.8 (29.6, 32.0)	1,398	2,365	45.3 (43.9, 46.8)
Any DA*	12,927	11,031	1,260	9.9 (9.4, 10.5)	7,096	3,046	26.0 (25.2, 26.8)	3,315	4,119	39.9 (38.9, 40.9)
Accident-related	259,862	227,489	16,759	6.6 (6.5, 6.7)	147,782	38,762	16.8 (16.7, 17.0)	64,240	54,292	28.3 (28.1, 28.6)
Boys: 15-17 years										
Adversity-related	57,706	48,560	5,452	9.7 (9.4, 9.9)	27,525	13,523	27.1 (26.7, 27.5)	11,394	17,349	40.3 (39.8, 40.8)
Any V*	27,177	23,993	1,781	6.7 (6.4, 7.0)	13,971	5,433	23.1 (22.5, 23.6)	5,400	7,267	36.7 (36.0, 37.4)
Any SI*	17,747	13,980	2,509	14.6 (14.0, 15.1)	7,337	5,229	34.1 (33.4, 34.9)	3,222	6,369	47.0 (46.1, 47.9)
Any DA*	32,281	26,050	3,662	11.7 (11.4, 12.1)	14,435	8,311	30.0 (29.5, 30.6)	6,251	10,436	43.2 (42.5, 43.9)
Accident-related	137,044	121,002	8,936	6.6 (6.5, 6.8)	75,558	23,588	19.6 (19.4, 19.8)	30,953	32,326	31.8 (31.5, 32.1)
Boys: 18-19 years										
Adversity-related	69,076	56,328	7,736	11.5 (11.3, 11.8)	30,077	18,131	30.5 (30.1, 30.8)	12,813	21,784	41.5 (41.0, 42.0)
Any V*	32,981	28,463	2,636	8.2 (7.9, 8.5)	15,994	7,370	25.7 (25.2, 26.3)	6,427	9,168	36.8 (36.2, 37.5)
Any SI*	20,352	15,449	3,521	17.8 (17.3, 18.4)	7,551	7,087	39.9 (39.2, 40.7)	3,490	8,171	50.8 (49.9, 51.6)
Any DA*	40,326	31,169	5,317	13.7 (13.4, 14.1)	15,643	11,540	34.0 (33.4, 34.5)	6,905	13,554	45.0 (44.4, 45.6)
Accident-related	86,450	76,022	6,514	7.7 (7.5, 7.8)	46,494	17,338	22.6 (22.3, 22.9)	19,984	22,194	33.1 (32.7, 33.5)
Boys: All										
Adversity-related	151,083	125,785	15,317	10.4 (10.2, 10.6)	70,723	36,928	28.2 (27.9, 28.4)	29,931	46,284	40.5 (40.2, 40.9)
Any V*	70,719	61,708	5,146	7.4 (7.2, 7.6)	35,699	14,770	24.0 (23.7, 24.4)	14,107	19,159	36.6 (36.1, 37.0)
Any SI*	44,740	34,856	6,850	15.8 (15.4, 16.1)	18,131	14,145	36.2 (35.8, 36.7)	8,110	16,905	48.5 (47.9, 49.1)
Any DA*	85,534	68,250	10,239	12.4 (12.2, 12.6)	37,174	22,897	31.2 (30.9, 31.5)	16,471	28,109	43.5 (43.1, 44.0)
Accident-related	483,356	424,513	32,209	6.8 (6.7, 6.8)	269,834	79,688	18.7 (18.5, 18.8)	115,177	108,812	30.2 (30.0, 30.3)

*Adolescents with records of any violent, self-inflicted or any drug/alcohol-related injury, respectively, at their index admission, are not mutually exclusive. ‘Re-admitted’ refers to re-admission as an emergency. V = violent, SI = self-inflicted, DA = drug/alcohol-related

G.5 Relative risks of emergency re-admission for girls and boys within ten years of discharge from index admission, by adjustment for potential confounding factors

Girls: emergency re-admission	Hazard ratio (95% Confidence Interval)			
Variables at index	**Unadjusted**	**Adjusted for age**	**Adjusted for age, chronic condition status**	**Adjusted for age, chronic condition status, ethnicity, deprivation**
Adversity-related (vs. Accident-related) injury	1.90 (1.88, 1.93)	1.76 (1.74, 1.79)	1.73 (1.71, 1.75)	1.66 (1.64, 1.69)
Age-group (vs. 10-14 years):				
15-17 years	. .	1.22 (1.20, 1.23)	1.20 (1.18, 1.21)	1.19 (1.17, 1.20)
18-19 years	. .	1.29 (1.27, 1.31)	1.24 (1.23, 1.26)	1.25 (1.23, 1.27)
Chronic condition (vs. None)	. .	. .	2.21 (2.19, 2.24)	2.00 (1.98, 2.02)
Ethnicity (vs. White):				
Black	. .	. .	. .	0.81 (0.78, 0.84)
Asian	. .	. .	. .	0.79 (0.76, 0.81)
Mixed	. .	. .	. .	0.99 (0.94, 1.04)
Other	. .	. .	. .	0.72 (0.68, 0.75)
Missing	. .	. .	. .	0.19 (0.18, 0.19)
Deprivation quintile (vs. Least deprived):				
2nd least deprived	. .	. .	. .	1.07 (1.05, 1.09)
Middle quintile	. .	. .	. .	1.14 (1.11, 1.16)
2nd most deprived	. .	. .	. .	1.22 (1.20, 1.25)
Most deprived	. .	. .	. .	1.32 (1.30, 1.35)
Missing	. .	. .	. .	0.21 (0.18, 0.24)

Boys: emergency re-admission	Hazard ratio (95% Confidence Interval)			
Variables at index	**Unadjusted**	**Adjusted for age**	**Adjusted for age, chronic condition status**	**Adjusted for age, chronic condition status, ethnicity, deprivation**
Adversity-related (vs. Accident-related) injury	1.52 (1.50, 1.53)	1.41 (1.39, 1.43)	1.36 (1.35, 1.38)	1.34 (1.33, 1.36)
Age-group (vs. 10-14 years):				
15-17 years	. .	1.14 (1.13, 1.15)	1.16 (1.15, 1.17)	1.16 (1.14, 1.17)
18-19 years	. .	1.26 (1.24, 1.27)	1.29 (1.27, 1.31)	1.30 (1.28, 1.32)
Chronic condition (vs. None)	. .		2.21 (2.19, 2.24)	1.96 (1.94, 1.99)
Ethnicity (vs. White):				
Black	. .	. .	. .	0.81 (0.78, 0.83)
Asian	. .	. .	. .	0.83 (0.80, 0.85)
Mixed	. .	. .	. .	0.94 (0.89, 0.99)
Other	. .	. .	. .	0.73 (0.70, 0.77)
Missing	. .	. .	. .	0.27 (0.27, 0.28)
Deprivation quintile (vs. Least deprived):				
2nd least deprived	. .	. .	. .	1.07 (1.05, 1.09)
Middle quintile	. .	. .	. .	1.14 (1.12, 1.16)
2nd most deprived	. .	. .	. .	1.23 (1.21, 1.25)
Most deprived	. .	. .	. .	1.35 (1.33, 1.37)
Missing	. .	. .	. .	0.23 (0.21, 0.25)

All variables were entered simultaneously into a semi-parametric proportionak hazards model (multi-variable results).

H. Supplementary results: Study III

H.1 10y cumulative risks of deaths after discharge of index admission, by sex, age-group, type of injury at index admission, and cause of death

Sex: age-group Index injury	N	Total deaths		Adversity-related death*		Suicide		DA death		Accidental death		Other death	
Girls: 10-15 years	151,141	3.5	(3.2, 3.9)	1.0	(0.8, 1.2)	0.5	(0.4, 0.6)	0.6	(0.5, 0.8)	0.7	(0.6, 0.9)	1.8	(1.5, 2.0)
Accident-related	103,215	2.9	(2.5, 3.3)	0.3	(0.2, 0.4)	0.1	(0.0, 0.2)	0.1	(0.1, 0.2)	0.6	(0.4, 0.8)	2.1	(1.8, 2.4)
Adversity-related	47,926	4.8	(4.1, 5.7)	2.7	(2.1, 3.4)	1.3	(1.0, 1.8)	1.7	(1.3, 2.3)	1.1	(0.8, 1.5)	1.0	(0.8, 1.4)
Self-inflicted	32,309	5.1	(4.2, 6.3)	3.2	(2.5, 4.2)	1.6	(1.1, 2.3)	2.2	(1.6, 3.1)	1.2	(0.8, 1.8)	0.7	(0.4, 1.2)
Violent	3,923	4.3	(2.4, 7.6)	2.2	(0.9, 5.3)	0.0	(0.0, 0.0)	1.6	(0.6, 4.3)	0.6	(0.2, 2.4)	1.5	(0.6, 3.6)
DA	41,973	4.7	(4.0, 5.6)	2.6	(2.0, 3.3)	1.4	(1.0, 1.9)	1.6	(1.1, 2.2)	1.2	(0.9, 1.7)	0.9	(0.6, 1.3)
Girls: 16-17 years	121,229	6.2	(5.6, 6.8)	3.2	(2.8, 3.7)	1.8	(1.5, 2.1)	1.9	(1.6, 2.3)	0.9	(0.7, 1.1)	2.0	(1.7, 2.4)
Accident-related	36,624	5.0	(4.2, 6.1)	1.5	(1.0, 2.1)	0.8	(0.5, 1.4)	0.7	(0.4, 1.3)	0.8	(0.5, 1.3)	2.8	(2.2, 3.6)
Adversity-related	84,605	6.7	(6.0, 7.5)	4.1	(3.5, 4.7)	2.2	(1.8, 2.7)	2.4	(2.0, 2.9)	0.9	(0.7, 1.2)	1.7	(1.4, 2.2)
Self-inflicted	63,520	6.8	(6.0, 7.8)	4.3	(3.7, 5.1)	2.5	(2.1, 3.1)	2.4	(1.9, 3.0)	0.9	(0.7, 1.3)	1.6	(1.2, 2.1)
Violent	5,269	8.1	(5.4, 12.0)	2.8	(1.5, 5.3)	1.2	(0.5, 3.3)	2.0	(1.0, 4.3)	1.5	(0.6, 3.7)	3.8	(2.0, 7.0)
DA	77,164	6.4	(5.7, 7.2)	4.0	(3.4, 4.6)	2.1	(1.7, 2.6)	2.4	(2.0, 3.0)	0.8	(0.6, 1.1)	1.6	(1.3, 2.1)
Girls: 18-19 years	76,018	9.1	(8.3, 10.1)	4.9	(4.3, 5.6)	3.1	(2.6, 3.6)	2.5	(2.0, 3.0)	1.3	(1.0, 1.7)	3.0	(2.5, 3.5)
Accident-related	26,623	5.7	(4.7, 6.9)	1.8	(1.3, 2.6)	1.0	(0.7, 1.6)	1.0	(0.6, 1.6)	1.4	(0.9, 2.1)	2.5	(1.8, 3.4)
Adversity-related	49,395	11.1	(10.0, 12.4)	6.6	(5.7, 7.6)	4.2	(3.5, 5.0)	3.3	(2.7, 4.1)	1.3	(0.9, 1.8)	3.2	(2.6, 4.0)
Self-inflicted	35,910	11.9	(10.5, 13.5)	7.3	(6.2, 8.6)	4.8	(4.0, 5.9)	3.5	(2.8, 4.4)	1.3	(0.8, 1.9)	3.4	(2.7, 4.3)
Violent	4,070	6.1	(3.6, 10.5)	4.0	(2.0, 7.9)	1.9	(0.8, 4.3)	2.4	(0.9, 6.2)	1.2	(0.4, 3.2)	1.0	(0.2, 4.3)
DA	44,751	11.2	(10.0, 12.6)	6.7	(5.7, 7.7)	4.3	(3.6, 5.2)	3.3	(2.7, 4.1)	1.2	(0.9, 1.8)	3.3	(2.7, 4.1)

Girls: All	348,388	5.6	(5.3, 5.9)	2.6	(2.4, 2.8)	1.5	(1.3, 1.6)	1.4	(1.3, 1.6)	0.9	(0.8, 1.1)	2.1	(1.9, 2.3)
Accident-related	166,462	3.8	(3.4, 4.2)	0.8	(0.6, 0.9)	0.4	(0.3, 0.5)	0.4	(0.3, 0.5)	0.8	(0.6, 0.9)	2.3	(2.0, 2.6)
Adversity-related	181,926	7.3	(6.8, 7.9)	4.4	(4.0, 4.8)	2.5	(2.2, 2.8)	2.5	(2.2, 2.8)	1.1	(0.9, 1.3)	1.9	(1.7, 2.2)
Self-inflicted	131,739	7.8	(7.2, 8.4)	4.8	(4.4, 5.4)	2.9	(2.6, 3.3)	2.7	(2.3, 3.1)	1.1	(0.9, 1.3)	1.8	(1.6, 2.2)
Violent	13,262	6.4	(4.8, 8.4)	3.0	(2.0, 4.6)	1.1	(0.6, 2.0)	2.0	(1.2, 3.4)	1.1	(0.6, 2.1)	2.2	(1.4, 3.6)
DA	163,888	7.2	(6.7, 7.8)	4.3	(3.9, 4.7)	2.5	(2.2, 2.8)	2.4	(2.1, 2.8)	1.1	(0.9, 1.3)	1.9	(1.6, 2.2)

Sex: age-group Index injury	N	Total deaths		Adversity-related death*		Suicide		DA death		Accidental death		Other death	
Boys: 10-15 years	284,163	4.9	(4.6, 5.3)	1.6	(1.4, 1.8)	0.8	(0.7, 1.0)	0.6	(0.5, 0.8)	1.5	(1.3, 1.7)	1.9	(1.7, 2.1)
Accident-related	259,862	4.5	(4.2, 4.9)	1.3	(1.2, 1.6)	0.7	(0.6, 0.8)	0.5	(0.4, 0.7)	1.4	(1.2, 1.6)	1.8	(1.6, 2.0)
Adversity-related	24,301	9.3	(7.8, 11.0)	4.5	(3.5, 5.7)	2.3	(1.6, 3.2)	1.9	(1.3, 2.7)	2.4	(1.7, 3.3)	2.5	(1.8, 3.4)
Self-inflicted	6<621	10.5	(7.8, 14.2)	7.1	(5.0, 10.2)	3.5	(2.1, 5.8)	3.2	(1.9, 5.5)	1.5	(0.7, 3.5)	1.9	(0.9, 3.9)
Violent	10,549	6.6	(4.8, 9.1)	2.7	(1.6, 4.5)	1.6	(0.9, 3.0)	0.9	(0.4, 2.2)	2.2	(1.3, 3.8)	1.7	(0.9, 3.2)
DA	12,925	11.2	(9.1, 13.7)	5.6	(4.2, 7.5)	3.0	(2.0, 4.4)	2.4	(1.6, 3.8)	2.7	(1.8, 4.1)	2.9	(2.0, 4.2)
Boys: 16-17 years	194,750	9.2	(8.6, 9.7)	4.9	(4.5, 5.3)	2.5	(2.3, 2.8)	2.5	(2.2, 2.8)	2.2	(2.0, 2.5)	2.1	(1.8, 2.4)
Accident-related	137,044	7.1	(6.5, 7.7)	3.0	(2.6, 3.4)	1.5	(1.2, 1.7)	1.5	(1.2, 1.8)	2.0	(1.7, 2.3)	2.1	(1.8, 2.4)
Adversity-related	57,706	14.4	(13.2, 15.7)	9.7	(8.7, 10.8)	5.1	(4.4, 5.9)	4.9	(4.2, 5.8)	2.7	(2.2, 3.3)	2.0	(1.6, 2.6)
Self-inflicted	17,708	22.6	(20.0, 25.7)	16.3	(14.1, 18.9)	10.1	(8.4, 12.1)	7.8	(6.3, 9.7)	3.3	(2.3, 4.6)	3.2	(2.2, 4.5)
Violent	27,129	8.7	(7.3, 10.2)	5.2	(4.2, 6.4)	2.0	(1.5, 2.8)	2.6	(1.8, 3.5)	2.1	(1.5, 2.9)	1.4	(0.9, 2.2)
DA	32,246	18.9	(17.0, 20.9)	13.6	(12.0, 15.4)	7.7	(6.6, 9.0)	7.0	(5.8, 8.3)	3.0	(2.3, 3.8)	2.4	(1.8, 3.2)
Boys: 18-19 years	155,526	13.2	(12.5, 13.9)	8.2	(7.7, 8.8)	3.9	(3.5, 4.3)	4.8	(4.3, 5.3)	2.6	(2.4, 3.0)	2.4	(2.0, 2.7)
Accident-related	86,450	8.8	(8.0, 9.6)	4.3	(3.8, 4.9)	2.3	(1.9, 2.7)	2.1	(1.7, 2.5)	2.5	(2.1, 2.9)	2.0	(1.6, 2.4)
Adversity-related	69,076	19.2	(17.8, 20.6)	13.6	(12.4, 14.8)	6.1	(5.4, 6.9)	8.5	(7.6, 9.5)	2.8	(2.4, 3.4)	2.8	(2.3, 3.5)
Self-inflicted	20,292	30.4	(27.4, 33.7)	23.1	(20.5, 26.0)	11.8	(10.0, 13.8)	14.0	(12.0, 16.4)	3.6	(2.6, 4.8)	3.9	(2.9, 5.4)
Violent	32,916	11.9	(10.5, 13.6)	7.6	(6.4, 9.0)	3.1	(2.4, 4.0)	4.5	(3.6, 5.6)	2.5	(1.9, 3.2)	1.9	(1.4, 2.7)
DA	40,250	25.1	(23.1, 27.3)	18.4	(16.7, 20.3)	8.4	(7.3, 9.6)	11.8	(10.4, 13.4)	3.3	(2.6, 4.1)	3.6	(2.8, 4.5)

Boys: All	634,439	8.2	(7.9, 8.5)	4.2	(4.0, 4.4)	2.1	(1.9, 2.2)	2.2	(2.0, 2.3)	2.0	(1.9, 2.1)	2.0	(1.9, 2.2)
Accident-related	483,356	6.0	(5.7, 6.3)	2.3	(2.2, 2.5)	1.2	(1.1, 1.3)	1.1	(1.0, 1.2)	1.8	(1.6, 1.9)	1.9	(1.8, 2.1)
Adversity-related	151,083	15.6	(14.8, 16.5)	10.5	(9.8, 11.2)	5.1	(4.6, 5.6)	5.9	(5.4, 6.5)	2.7	(2.4, 3.1)	2.5	(2.1, 2.8)
Self-inflicted	44,621	24.2	(22.4, 26.1)	17.9	(16.3, 19.5)	9.8	(8.7, 11.0)	9.8	(8.7, 11.1)	3.1	(2.5, 3.9)	3.3	(2.7, 4.1)
Violent	70,594	9.9	(8.9, 10.9)	5.9	(5.2, 6.7)	2.5	(2.0, 3.0)	3.2	(2.7, 3.8)	2.3	(1.9, 2.8)	1.7	(1.3, 2.2)
DA	85,421	20.3	(19.1, 21.6)	14.3	(13.3, 15.4)	7.2	(6.5, 8.0)	8.3	(7.5, 9.2)	3.1	(2.7, 3.6)	3.0	(2.5, 3.5)

Data presented as risk per 1,000 (95% Confidence Interval), unless otherwise stated.
*Suicides, homicides and drug/alcohol-related deaths. These deaths were not mutually exclusive. Risks are not reported for homicides due to small counts.

I Research profile

I.1 Publications during Sept 2012-July 2016, that do not form part of this thesis

Publications resulting from the work of this thesis are presented in Appendix D. In addition, as part of the Royal Statistical Society's annual writing competition, I used Naïve Bayesian Classifiers to try to predict the winners of the television series 'The Great British Bake off', which came runner-up. The article was published in their online magazine, *Significance*, in December 2015:

https://www.statslife.org.uk/culture/2602-the-great-british-bayes-off-how-much-difference-statistically-does-a-soggy-bottom-make

I, along with Dr. Leah Li, Prof. Ruth Gilbert, Dr. Arturo Gonzalez-Izquierdo, and Ms. Janice McGhee, published a comparison of time-trends of the incidence of admissions for adversity-related injury during adolescence, between England and Scotland, in the *Journal of Public Health*, in February 2016 (215).

I, along with Dr. Pia Hardelid, Dr. Linda Wijlaars, Miss Ania Zylbersztejn, and Dr. David Cromwell, recently wrote a 'data profile' about Hospital Episode Statistics. The article is currently under review with the *International Journal of Epidemiology*.

I.2 Presentations

I have presented the work of this thesis at several conferences and workshops, within UCL, nationally, and internationally.

The results of Study I (Chapter 4) were presented at:

- Scottish Health Informatics Programme conference 2013 (oral)
- UCL Institute of Child Health Open Day 2013 (poster)

- Farr internal seminar (oral)
- UCL Alcohol Research Interests Group (oral)
- Frontiers in Population Health conference 2014 (poster)
- UCL poster competition 2014

Statistical methods discussed in Chapter 5 were presented at:

- Survival Analysis for Junior Researchers conference 2014 (oral)
- International Society of Clinical Biostatistics conference 2015 (poster)
- Royal Statistical Society International conference 2015 (oral)
- Society for Longitudinal and Life-course studies conference 2015 (oral)

The results of Study II (Chapter 6) were presented at:

- Public Health Science conference 2014 (poster). The abstract was published in a Lancet supplementary series (http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736%2814%2962162-0.pdf)
- International Mental Health Congress 2015 (oral)
- Farr International conference 2015 (oral)
- Department of Health Child Policy Research Unit conference 2015 (invited oral)

The results of Study III (Chapter 7) will be presented at:

- International Population Data Linkage conference 2016 (poster)
- Department of Health Child Policy Research Unit conference 2017 (invited oral)

I.3 Training

I attended several internal and external training during my time as a PhD student, including:

- Internal UCL courses on data linkage (Feb 2013), Bayesian analysis (April 2013), multi-level modelling (Aug 2013), and longitudinal data analysis (June 2014), using MySQL (March 2015)
- ThinkWrite® courses on 'Conference abstracts and posters', 'Planning and writing your thesis', 'Quality papers: how to write papers that can be published in your target journals', and 'Writing science for the public' (May 2014, Jan 2015)
- The MRC Cambridge Biostatistics course 'Introduction to Bayes using BUGS' (Oct 2013)

I improved my communication skills through several avenues, including as

- mentor of 16 first and second year PhD students (2013-2015)
- point of contact for A-level students in our department who participated in the In2Science® internship scheme (Summer 2013-2015)
- facilitator at the Farr Soundboard event, which included two days' training in communication and facilitation (Nov 2014)
- assistant tutor in the Centre for Evidence-based Child Health's course in evidence-based medicine (Nov 2012, June 2013) and in the Administrative Data Research Centre's courses in 'Introduction to Data Linkage' (Sept 2014, March 2015)

I have also attended training in data governance, including the Administrative Data Liaison Service Safe Researcher course (June 2013), and UCL mandatory information governance training (June 2015).

I became more involved with the Royal Statistical Society, becoming a committee member of the Young Statisticians Section, Medical Section, and Publications Network. As a member of the Medical Section, I have personally organised workshops of ‘Classification methods and applications in big databases’ (December 2014), ‘The use of technology and web resources in teaching statistics’ (September 2015), and ‘Recent developments in growth assessment: the LMS method, GAMLSS and beyond’ (February 2016).

Finally, I hope to carry forward the findings of this thesis as part of a mixed methods study, led by Dr. Jamie Murdoch of the University of East Anglia. We are currently planning a qualitative study in adolescents, hospital workers, and youth workers, to determine the feasibility of placing youth workers in the emergency department to support adolescents with adversity-related injury and potentially reduce risks of future harm. To inform this planning, I recently co-led (alongside Dr. Murdoch) a two-hour session with seven members of the National Children’s Bureau’s Families Research Advisory Group (including parents, a foster carer, a midwife, and school governors). We discussed the feasibility of interventions delivered to adolescents who present to hospital with adversity-related injury, and the potential mechanisms of effective interventions.

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